Australian National University

Type 2 diabetes mellitus in transitional Thailand: incidence, risk factors, mediators, and implications

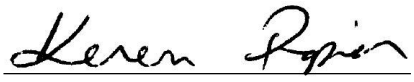
Keren Papier

December 2017

A thesis submitted for the degree of Doctor of Philosophy of
The Australian National University

Declaration

I declare that the work contained in this thesis is the result of my original research and has not been submitted to any other University or Institution. This thesis was undertaken between March 2014 and December 2017 as a PhD Candidate enrolled at the Australian National University.



Keren Papier

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Acknowledgments

Numerous individuals deserve recognition for their guidance, support, and encouragement, without which this research would not have been completed.

First, I would like to thank my principal supervisor Adrian Sleigh, who continually supported the development of my research and professional skills and was there for me when I needed guidance but also allowed me to have space to work independently. The other members of my supervisory panel were similarly supportive. Susan Jordan, with her door always open, has spent countless hours assisting me with all aspects of this research, provided ongoing support, encouragement and technical expertise, and encouraged me to be an active thinker. Cate D'este showed patience without measure, motivated me to embark on new analytical adventures, and always supported with interpretation. Chris Bain, with his remarkable ability to think outside the box, has challenged me to understand what I am doing and to think critically. Sam-ang Seubsman, who assisted with my field work in Thailand, supported all aspects of my research; without her this work would not have been possible. Cathy Banwell whose positive attitude, wisdom, and advice helped guide me forward. And Vasoontara Yiengprugsawan, who has been supportive and encouraging throughout the duration of this research.

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To my wonderful colleagues in the Thai Health-Risk Transition Study, I feel truly lucky to have met you all and to have been a part of this extraordinary cohort. To the wonderful friends I made during my candidature, Suni, Liz, Jean-Claude, Lena, Annika, Mary, Ellie, Katie, Suzy, Libby, Jenny, Rimante, thank you for making this experience so memorable.

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Abstract

Background

Economic growth in Asia is changing population health profiles. Family structures, environments, occupations, education, and health behaviours have also changed and science-based health services have evolved. As part of this 'health-risk transition', non-communicable diseases including type 2 diabetes mellitus (T2DM) have emerged. While the major causes of the diabetes epidemic in western, high-income countries are well documented, little is known of T2DM in developing Asia. The knowledge gap includes Thailand, which needs to identify local factors driving its T2DM epidemic.

Aim

This thesis aims to better understand the epidemiology of T2DM emerging in Southeast Asia.

Methods

Participants were from the Thai Cohort Study (TCS) of the health-risk transition. They were distance-learning adult students living all over Thailand, enrolled at Sukhothai Thammithirat Open University, and surveyed in 2005, 2009, and 2013 using mailed questionnaires that covered socio-demographic characteristics, lifestyle behaviours and self-reported health outcomes. In addition to these data, physician telephone interviews were conducted to validate self-reported questionnaire responses (2015); and a dietary survey was conducted to assess transitional dietary patterns (2015).

Multiple logistic regression was used to calculate odds ratios and 95% confidence intervals (CIs) for longitudinal associations between exposures of interest and T2DM. Non-linear associations of body mass index (BMI) and T2DM were modelled using restricted cubic splines. Counterfactual mediation analysis explored sugary drink linkage to T2DM. Population attributable fractions and potential impact fractions were calculated. Principal component analysis identified dietary patterns and multivariable linear regression produced standardized coefficients and 95% CIs for associations between socio-demographic measures and dietary pattern scores.

Results

Physician telephone interviews of a cohort sample demonstrated high validity of questionnaire self-reported doctor diagnosed T2DM suggesting that self-reported doctor diagnosed T2DM is a feasible and acceptable method for assessing diabetes in epidemiological studies.

Overall eight-year T2DM incidence was 177 per 10 000 (95% CI 164-190) with higher incidence in men. For both sexes, factors most strongly associated with T2DM risk were greater age and BMI. Two-thirds of all T2DM cases could be attributed to overweight and obesity. T2DM risk increased at BMI levels <23kg/m^2. The increasing T2DM risk associated with body size became statistically significant at a BMI of 22 kg/m^2 and 20 kg/m^2 in men and women, respectively. For both sexes, living in urban areas increased T2DM and risk of consuming unhealthy dietary patterns, while a higher income associated with healthy dietary patterns. In Thai men, smoking and alcohol consumption increased T2DM risk. In women, sugary-drink consumption increased T2DM risk, of which 23% was mediated through obesity. In men, income and education were associated with increased T2DM risk. In women, education protected against unhealthy dietary intake. Overall, women tended to have safer behaviours (e.g. low prevalence of smoking and alcohol consumption) and better outcomes (e.g. lower prevalence of obesity and lower rates of T2DM).

Conclusions

Findings from young to middle-aged, educated Thai adults nationwide show that self-report of incident T2DM is a valid method for assessing diabetes in epidemiological studies, T2DM incidence in Thailand is high, and accompanying lifestyle and socio-demographic transitions are driving the T2DM epidemic. Thai men are likely to be in the middle stages of the health-risk transition while women are more advanced. Health-risks for T2DM are changing substantially and could be modified. These risks need to be targeted to prevent and control diabetes in Thailand.

Table of Contents

List of Tables

*Tables and figures included in the results chapters 3-7 are integrated into the publications and are not listed here

List of Figures

Publications, presentations awards and activities

This thesis by compilation is based on the following five original publications to which I have made the main contribution as first author.

Peer reviewed publications during candidature that are included in this thesis

1) **Papier, K.,** Jordan, S., Bain, C., D'este, C., Thawornchaisit, P., Seubsman, S. and Sleigh, A., 2016. Validity of Self-Reported Diabetes in a Cohort of Thai Adults. *Global Journal of Health Science, 9*(7), p.1.

2) **Papier, K.,** Jordan, S., Catherine, D.E., Bain, C., Puengson, J., Banwell, C., Yiengprugsawan, V., Seubsman, S., and Sleigh, A., 2016. Incidence and risk factors for type 2 diabetes mellitus in transitional Thailand: results from the Thai cohort study. *BMJ open*, *6*(12), p.e014102.

3) **Papier, K**., D'Este, C., Bain, C., Banwell, C., Seubsman, S., Sleigh, A., and Jordan, S. (2017). Consumption of Sugar Sweetened Beverages and Type 2 Diabetes Incidence in Thai Adults: Results from an Eight Year Prospective Study. *Nutrition & Diabetes, 7*(6), p.e283.

4) **Papier, K**., D'Este, C., Bain, C., Banwell, C., Seubsman, S., Sleigh, A., and Jordan, S. (2017). Body mass index and type 2 diabetes in Thai adults: defining risk thresholds and population impacts. *BMC Public Health*, *17*(1), p.707.

5) **Papier, K**., Jordan, S., D'Este, C., Banwell, C., Yiengprugsawan, V., Seubsman, S., Sleigh, A. (2017). Social Demography of Transitional Dietary Patterns in Thailand: Prospective Evidence from the Thai Cohort Study. *Nutrients. 9*(11), p.1173.

In relation to the thesis I also co-authored another publication reproduced in Appendix D cited as follows

> Yiengprugsawan, V., Rimpeekool, W., **Papier, K.**, Banwell, C., Seubsman, S.A., and Sleigh, A.C. 2017. Relationship between 8-year weight change, body size, and health in a large cohort of adults in Thailand. *Journal of Epidemiology*, 2*7*(10), p. 499.

As well, I have produced seven conference presentations using the research within this thesis and engaged with the media extensively for publication number three. I also received two awards and four scholarships, and was selected to attend four courses including one international course at Imperial College London in the UK.

Conference presentations

1) Body mass index and diabetes in Thai adults: thresholds and impacts. *Australasian Epidemiological Association (AEA) 30th Anniversary Meeting,* Australia, September 2017 (**Oral presentation**)

2) Consumption of Sugar Sweetened Beverages and Type 2 Diabetes Incidence in Thai Adults: Results from an Eight Year Prospective Study. *15th World Congress on Public Health*, Australia, April 2017 (**Oral presentation**).

3) Consumption of Sugar Sweetened Beverages and Type 2 Diabetes Incidence in Thai Adults: Results from an Eight Year Prospective Study. *Australia and New Zealand Obesity Society (ANZOS).* Brisbane, Australia. October 2016 (**Oral presentation**).

4) Incidence and Risk Factors of Type 2 Diabetes Mellitus in Transitional Thailand. *21th Biennial Conference (Asian Studies Association of Australia, ASAA 2016)*. Canberra, Australia, July 2016 (**Oral presentation**).

5) Validity of diabetes self-reports in the Thai Cohort Study: comparison with physician telephone interviews. *Nutrition Higher Degree Research (HDR) Summit*. Brisbane, Australia, December, 2015 (**Oral presentation**).

6) Incidence and Risk Factors of Type 2 Diabetes in Transitional Thailand. *The Nutrition Society of Australia and New Zealand Annual Scientific Meeting*. Wellington, New Zealand, December, 2015 (**Poster presentation**).

7) Incidence of Type 2 Diabetes in Transitional Thailand. ICDAM9 9th International Conference on Diet and Activity Methods, Brisbane. Australia, September, 2015 (**Poster presentation**).

Media

In Appendix F, I include a media report summary for the coverage of '*Consumption of Sugar Sweetened Beverages and Type 2 Diabetes Incidence in Thai Adults: Results from an Eight Year Prospective Study'* featured across several national news programs in Australia (463 media reports, audience of 6 million).

Awards and scholarships

1) 2017 Emerging Media Talent Award nominee, Australian National University

2) 2016 Australian and New Zealand Obesity Society (ANZOS) Public Health Early Career Researcher Award (AU $250)

3) 2016 Vice-Chancellor's HDR Travel Grant, ANU (AU $1500)

4) 2015 Travel award, Public health association of Australia (International health) (AU$1000)

5) 2015 Travel bursary, ARC Centre of Excellence in Populations Aging Research, Australian National University (AU$750)

6) 2014-2017 Australian Postgraduate Award, ANU

Courses

1) 2017 Advanced Epidemiology Short Course, University of Sydney

2) 2016 6th International Course in Nutritional Epidemiology, Imperial College London

3) 2016 Communicating Science, Australian National University

4) 2015 Longitudinal Data Analysis Workshops, Australian National University

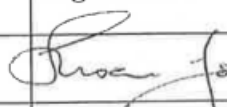
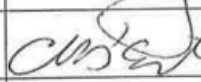
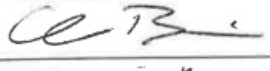
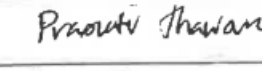
Contribution declaration for publications

My contribution to each of the five thesis papers on which I was first author follows:

I devised each of the five studies, analysed all of the data in consultation with my supervisory team, drafted the manuscripts, and coordinated co-author input including interpretation of the results for each paper. I undertook revisions to the manuscript based on peer review feedback and managed the submission process. In addition to the above contribution, for the validation study and the dietary study, I constructed the interview protocol and the dietary survey in consultation with my supervisory team, submitted the human research ethics application documents, mailed out interview invitations and dietary surveys to all study participants, and managed the collection and processing of all collected data. I also sought permission from a representative from the Thai Ministry of Public Health to use the Thai National Health Examination Survey food frequency questionnaire for this study.

Collaborating authors

I agree that Keren Papier contributed to the authorship and research of her thesis paper(s) on which I am a co-author, as stated above.

Author name	Signature	Date
Susan Jordan		17/11/2017
Catherine D'este		23/11/2017
Chris Bain		23/11/2017
Prasutr Thawornchaisit		23. Nov 2017
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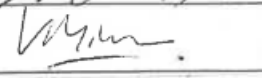
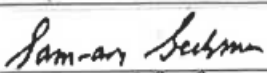
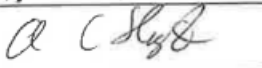
Vasoontara Yiengprugsawan		23/11/2017
Sam-ang Seubsman		23/11/2017
Adrian Sleigh		23/11/2017

Acronyms and abbreviations

ADA	American Diabetes Association
ASB	Artificially Sweetened Beverages
β	Beta
BMI	Body Mass Index
CI	Confidence Interval
DAG	Direct Acyclic Graph
DALYs	Disability Adjusted Life Years
FPG	Fasting Plasma Glucose
FFA	Free Fatty Acids
FFQ	Food Frequency Questionnaire
GWAS	Genome Wide Association Studies
GTT	Glucose Tolerance Test (modified)
GI	Glycemic Index
GL	Glycemic Load
GDP	Gross Domestic Product
GNP	Gross National Product
HBA1c	Glycated haemoglobin A1c
HIC	High Income Countries
IFG	Impaired Fasting Glucose (glycemia)
IGT	Impaired Glucose Tolerance
IDDM	Insulin-Dependent Diabetes Mellitus
IDF	International Diabetes Federation
ITF	International Task Force
Kcal	Kilocalories
Kg	Kilogram
LMICs	Low and Middle-Income Countries
MUFA	Monounsaturated Fatty Acids
NCDs	Non-Communicable Diseases
NDDG	National Diabetes Data Group
OR	Odds Ratio
OGTT	Oral Glucose Tolerance Test
PA	Physcial Activity

PAF	Population Attributable Fraction
PCA	Principle Component Analysis
PIF	Potential Impact Fraction
PUFA	Polyunsatured Faty Acids
RPG	Random Plasma Glucose Test
SFA	Saturated Fatty Acids
SEP	Socio-Economic Position
SEA	Southeast Asia
SSB	Sugar-sweetened beverages
STOU	Sukhothai Thammathirat Open University
NHES	Thai National Health Examination Surveys
TCS	Thai Cohort Study
TFA	Trans-Fatty Acids
T2DM	Type II Diabetes Mellitus
USD	United Stated Dollars
WHO	World Health Organization

1

INTRODUCTION

The global situation with diabetes has been summarized well by Jean Claude Mbanya, a prominent scholar in this field

> "No country is immune to the threat and no country is fully equipped to repel this common enemy alone. The coming fight will require a united stand with the full support of the international community, for this is a battle the world cannot afford to lose" (Mbanya, 2009).

Kofi Annan, former UN secretary general reinforces this view and adds his own perspective

> "Without tackling the diabetes epidemic which is now gripping our world, we will, I fear, find many of our ambitions for the future simply impossible to achieve" (Annan, 2008).

1 Introduction

This thesis reports my PhD research conducted over nearly four years at the Australian National University. The study addresses the topic of type 2 diabetes mellitus now emerging as an important population health problem in Southeast Asia. The thesis includes eight chapters and in this opening chapter I review the relevant literature, describe the aims and objectives of my study, and outline the structure of the thesis.

1.1 Overview

Chapter 1 commences with a description of the study setting and then proceeds to analyse the relevant literature beginning with the definition, pathophysiology and clinical features of type 2 diabetes (T2DM) (Section 1.3). Following this is an analysis of the evolution of the clinical methods used to diagnose T2DM over the past 50 years as well as the methods used to diagnose and validate diabetes in epidemiological field work (Section 1.4). The global trends in the incidence and prevalence of T2DM, the descriptive epidemiology of diabetes, and its burden in Southeast Asia and Thailand are also examined in Section 1.5. This chapter then investigates the known determinants of T2DM with a focus on the role of modifiable risk factors of T2DM (Section 1.6). The health-risk transition currently underway in Southeast Asia and Thailand and its role in the emergence of T2DM is also examined (Section 1.7). In Section 1.8, I summarize the current knowledge on the emerging T2DM epidemic in Southeast Asia and provide justification for this doctoral work. The aims, objectives, and research questions are presented in Section 1.9 and the Thesis structure is presented in Section 1.10.

1.2 Study setting

In recent decades, many low and middle-income countries (LMICs) have experienced rapid economic development. There have been many health benefits associated with this growth including increased life expectancy, falling maternal-child mortality, control of infectious diseases, and improved health services. But accompanying urbanization and industrialization have also induced a shift towards increasingly sedentary occupations with decreased energy expenditure, changes in dietary intake, and adoption of unhealthy behaviours. These changes led to the emergence of chronic diseases. Collectively, these

shifts in environment, behaviours, and diseases have been termed the 'Health-risk transition' (Sleigh et al., 2008) which is considered in Section 1.7.

As part of the health-risk transition, type 2 diabetes (T2DM) has emerged as a leading health and economic burden in many LMICs (World Health Organization, 2016). T2DM is an important risk factor for tuberculosis and cardiovascular disease, two diseases that already have a high burden in LMICs (NCD Risk Factor Collaboration, 2016). Furthermore, 75% of the world's adult population with diabetes now lives in LMICs (International Diabetes Federation, 2017), where the largest proportion of premature deaths attributable to T2DM under the age of 70 occurs (World Health Organization, 2016). In addition, around 60% of the global costs for T2DM are borne by LMICs (NCD Risk Factor Collaboration, 2016). With the number of adults with diabetes projected to increase to 629 million by 2045, and much of this rise expected to occur in Southeast Asia, the health and economic burden of T2DM is likely to increase.

Thailand is one such Southeast Asian country with rapidly emerging T2DM. Over the past three decades, the national prevalence of T2DM in Thailand has increased from 2.3% in 1991 to 8.9% in 2014 (Chavasit et al., 2017); making it the top cause of Disability Adjusted Life Years (DALYs) lost for Thai women and the seventh cause for men (Bundhamcharoen et al., 2011). Diabetes also imposes a substantial burden on the healthcare system in Thailand. Hospitalization rates for diabetes have risen from 33.3/100 000 population in 1985 to 586.8/100 000 population in 2006 (Ministry of Public Health Thailand, 2009). In 2008, the average annual cost per patient was USD $ 881, 21% of the per capita gross domestic product of Thailand in that same year (Chatterjee et al., 2011). These estimates were even higher among adults who experienced complications from T2DM (Deerochanawong and Ferrario, 2013).

While the epidemiology of T2DM and its risk factors in developed, high income countries is well documented, comparable information for Southeast Asian countries such as Thailand is limited. Data on T2DM distribution, incidence and risk factors are needed to better understand T2DM in Southeast Asia. Identifying local drivers of the emerging epidemic of T2DM in Southeast Asia will help identify prevention targets, guide policy and health planning, and provide useful foresight regarding future trends in T2DM in Southeast Asia.

1.3 Type 2 diabetes mellitus

1.3.1 Definition

Diabetes Mellitus is a heterogeneous metabolic disorder that is characterized by elevated levels of fasting and/or postprandial glucose in the blood (hyperglycaemia) (Qiao, 2012, Surampudi et al., 2009). People with diabetes have impaired glucose regulation which leads to disturbances in their metabolism of carbohydrate, fat and protein (Kahn et al., 2005). The majority of cases are either classified as 'Type 1' or 'Type 2'. These classifications are determined by aetiology (Goldstein and Müller-Wieland, 2013). Type 1 diabetes mellitus, previously referred to as 'insulin-dependent diabetes mellitus' (IDDM) (World Health Organization, 1980) is caused by autoimmune-mediated destruction of the islet beta (β) cells in the pancreas (Zimmet et al., 2001). It accounts for less than 10% of the global prevalence of diabetes and mostly affects children (International Diabetes Federation, 2015). Type 2 diabetes mellitus (T2DM), previously referred to as 'non-insulin-dependent diabetes mellitus' (NIDDM) (National Diabetes Data Group, 1979) and 'adult onset diabetes' is caused by the decreased sensitivity of skeletal muscle to insulin (insulin resistance) and/or by the decreased secretion of insulin by the β cells (Amos et al., 1997, McCrimmon et al., 2012). It accounts for over 90% of the global prevalence of diabetes (International Diabetes Federation, 2015). Although the risk and prevalence of T2DM increases with age (Guariguata et al., 2014), its age of onset has decreased over the past few decades with T2DM incidence now rising rapidly among children and adolescents globally (Lammi et al., 2007, Likitmaskul et al., 2003).

1.3.2 Pathophysiology

Chronic surfeit dietary intakes and obesity are the major drivers in the development of T2DM. In response to excess fuel intakes, the pancreatic β cells hyper-secrete insulin in order to maintain normoglycaemia. In some individuals, this compensation response eventually fails as the β cell function declines. This leads to a state of 'relative insulin deficiency', hyperglycaemia and the development of T2DM (Sutanegara and Budhiarta, 2000).

Obesity contributes to the development of T2DM through its ability to impair the functional action of insulin. Individuals who are obese have larger and higher numbers of adipose cells. These cells can release inflammatory cytokines like Tumour Necrosis

Factor, which adversely affects the insulin signalling cascade (Stumvoll et al., 2005). These cells can also release hormones like leptin that inhibits insulin secretion (Ramachandran et al., 2012). Finally, adipose cells also release plasma free fatty acids (FFAs) which stimulate gluconeogenesis and decrease peripheral glucose clearance by accumulating in the blood and interfering with the uptake of blood glucose by the muscle (Sutanegara and Budhiarta, 2000, Stumvoll et al., 2008). Furthermore, individuals with obesity have been found to have decreased concentrations of adiponectin, a protein that is released from adipose tissue and increases insulin sensitivity (Ramachandran et al., 2010, Lindsay et al., 2002, Nyamdorj, 2012).

1.3.3 Clinical Features

Before being diagnosed with T2DM, individuals usually experience a long period of asymptomatic hyperglycaemia that can last for many years. During this period, individuals experience 'impaired glucose regulation', the metabolic stage between normal glucose homeostasis and diabetes. Impaired glucose regulation is characterized by elevated postprandial blood glucose levels and/or fasting blood glucose levels that are higher than normal but lower than the levels used to diagnose diabetes. Elevated postprandial glucose, termed impaired glucose tolerance (IGT) and previously named 'subclinical and/or borderline diabetes', indicates mild degrees of glucose intolerance (Qiao, 2012). This is a reversible metabolic stage that puts the individual at an increased risk of T2DM. Elevated fasting blood glucose, termed impaired fasting glucose (IFG), is less prevalent than IGT. However, it is also associated with an increased risk of T2DM (Kahn et al., 2005, Stumvoll et al., 2005). Unlike IFG, which can be identified during a fasting state, IGT can only be identified through an oral glucose tolerance test (OGTT) where blood is measured both in a fasting state and after glucose consumption. A standard OGTT is administered by giving a 75g dose of glucose to an individual who has fasted overnight and then measuring their blood glucose 2 hours after this dose (Kahn et al., 2005, Unwin et al., 2002). Over time, IFG, IGT or both combined can lead to T2DM. This is because as a consequence of chronically high blood glucose, the pancreatic β cells may increase insulin secretion. The over production of insulin can then lead to the reduced function of the β cells and reduced insulin sensitivity, which may eventually result in a relative insulin deficiency and T2DM (Stumvoll et al., 2005).

Type 2 diabetes is associated with serious long-term health complications. Major health consequences of T2DM include micro and macro vascular diseases (Duckworth et al., 2009, Markku, 2008). The micro vascular diseases that are associated with hyperglycaemia include retinopathy, progressive renal disease and peripheral neuropathy (Coopan, 2008). The macro vascular diseases that are associated with hyperglycaemia include coronary artery and heart disease and peripheral vascular disease, which are the leading causes of mortality in people with diabetes (Coopan, 2008). There are many mechanisms by which elevated blood glucose can increase the risk of vascular disease. These include the effect of high blood glucose on vascular cell chemical changes (i.e the formation of glycosylation end products that bind to receptors and cause inappropriate signal transduction in vascular cells that leads to the release and excessive formation of oxidants) and/or the up regulation of enzymes (i.e. such as aldose reductase which increases levels of sorbitol and subsequently alters metabolic activity). Irrespective of the mechanism at play, diabetes significantly increases the risk of several major long-term health complications and this effect is predominantly attributed to hyperglycaemia (Coopan, 2008, Kahn et al., 2005).

1.3.4 Summary – T2DM

T2DM is a disabling, multi-system metabolic disorder with numerous manifestations. It has diverse health effects interfering with many vital functions that are needed for productive life. It shortens the life span and decreases the quality of life.

1.4 Diagnosing diabetes

1.4.1 Diagnostic criteria

The diagnosis of T2DM is complex due to the heterogeneous nature of this disorder and the long asymptomatic period of hyperglycaemia that precedes the clinical stages of T2DM. All diagnostic criteria are based on glycaemic levels that are measured using different assay methods (Qiao, 2012). In order to confirm diagnosis of diabetes, blood glucose measures must be repeated (American Diabetes Association, 2010, World Health Organization, 1999). The preferred measurement is plasma glucose with the reading done quickly before the specimen degrades. The different plasma glucose measures that can be used to diagnose diabetes and/or other categories of glucose tolerance include the following:

RPG (random plasma glucose test): taken at any time of the day without regard to the last meal consumed together with the reporting of classic symptoms of diabetes that include polyurea, polydipsea and unexplained weight loss and (Nolan et al., 2011);

FPG (fasting plasma glucose test): taken after an overnight fast or an 8 hour fast;

OGTT (oral glucose tolerance test) or 2 hour plasma glucose test: taken two hours after the ingestion of 75 grams of oral glucose (World Health Organization, 2006);

HbA1c (glycated haemoglobin A1c): a marker that reflects glycaemic levels over the preceding 2-3 month period (American Diabetes Association, 2013).

The diagnostic cut-offs of these blood glucose measures have varied slightly over the past few decades (Markku, 2008). In the late 1970's, the findings from several cross-sectional and longitudinal studies suggested that the development and progression of retinopathy only occurred in individuals who had a capillary blood glucose of 11.1mmol/l 2-hours after consuming 50g of glucose (otherwise known as a 'modified glucose tolerance test' (GTT). Consequently, these cross-sectional studies suggested that the 1965 World Health Organization (WHO) diagnostic cut offs for diabetes were set too low to detect complications associated with hyperglycaemia (Qiao, 2012, World Health Organization, 1965). In light of these findings, the American National Diabetes Data Group (NDDG) suggested that new diabetes diagnostic cut-offs be implemented in 1979 (National

Diabetes Data Group, 1979). In 1980, the NDDG diagnostic cut-offs for diabetes were adopted by the WHO with slight modification (World Health Organization, 1980) and then revised again in 1985 (World Health Organization, 1985). The 1979 and 1980 diagnostic criteria made it possible to distinguish between type 1 and type 2 diabetes based on clinical features and pathophysiology and enabled comparison from different sources with greater confidence attributed to the addition of diagnostic cut off values for both IGT and T2DM. The 1985 WHO cut-offs were administered world-wide without modification until 1997 (Qiao, 2012).

In 1997, the American Diabetes Association (ADA) expert committee recommended lowering the WHO 1985 FPG levels (see Table 1) based on data that showed that the incidence of diabetic retinopathy began at this level ($\geq$7.0mmol/l) and as a way to lower the discrepancy between cases detected by the FPG and the 2 hour plasma glucose in the OGTT. The ADA expert committee proposed that the OGTT was not necessary for clinical use as it was inconvenient and more expensive than the FPG. The ADA also introduced a new FPG diagnostic cut off for IFG. Finally, the ADA highlighted that the HbA1c was not recommended as a diagnostic tool for diabetes due to the lack of standardized methodology among laboratories (Genuth et al., 2003).

In 1999, the WHO revised their 1985 diagnostic cut-offs and lowered the FPG criteria for diabetes according to the 1997 ADA recommendations (World Health Organization, 1999). In 2003, the ADA further revised the 1997 ADA diagnostic cut-offs and recommended that the FPG cut offs for IFG also be lowered (see Table 1-1) (Genuth et al., 2003). Although the implications of this would be an increased prevalence of cases with IFG, the ADA argued that this would help to increase the sensitivity of predicting future diabetic cases and preventing complications (Genuth et al., 2003).

In 2009, following the 2008 international expert committee discussions held between members of the ADA, the International Diabetes Federation (IDF) and the European Association for the Study of Diabetes (EASD), the ADA revised the 2003 ADA diagnostic criteria to include Hba1c cut offs for diabetes and increased risk of diabetes (see Table 1-1) (American Diabetes Association, 2010). In 2011, the WHO accepted the recommended HbA1c cut-off points for diagnosing diabetes proposed by the ADA in 2010. However, the WHO stated that an HbA1c value below 6.5% would not exclude

diabetes that was diagnosed using the other glucose tests (World Health Organization, 2011b). Apart from the inclusion of the HbA1c, the current WHO cut-offs for diabetes and increased risk of diabetes have remained unchanged since 1999 (World Health Organization, 2011b) and together with the various ADA cut-offs are the most widely used criteria for diagnosing diabetes in both clinical settings and epidemiological studies worldwide (International Diabetes Federation, 2015, McNeely and Boyko, 2004).

Table 1-1 Trends in the diagnostic criteria for diabetes and categories of increased risk of diabetes

Clinical Stage	**Diagnostic criteria by organization and year**									
	WHO 1965	NDDG 1979	WHO 1980	WHO 1985	ADA 1997	WHO 1999	ADA 2003	WHO 2006	ADA 2009	WHO 2011
*2-h plasma glucose	>7.2†	>11.1	>11.0	>11.1	>11.1	>11.1	>11.1	>11.1	>11.1	>11.1
Fasting glucose	-	>7.8-11.0	>8.0	>7.8	>7.0	>7.0	>7.0	>7.0	>7.0	>7.0
Random plasma glucose	-	-	>11.0 +CS	>11.1 +CS	>11.1 +CS	>11.1 +CS	>11.1 +CS	>11.1 +CS	>11.1 +CS	>11.1 +CS
HbA1c %	-	-	-	-	-	-	-	-	>6.5	>6.5
Impaired glucose tolerance (IGT)										
*2-h plasma glucose	6.1-7.1	>7.8-11.0	>8.0-10.9	>7.8-11.0	>7.8-<11.1	>7.8 -<11.1	>7.8-<11.1	>7.8-<11.1	>7.8-<11.1	>7.8-<11.1
Fasting glucose	-	7.8	<8.0	<7.8	-	<7.0	-	<7.0	-	<7.0
Impaired fasting glucose (IFG)										
*2-h plasma glucose	-	-	-	-	-	<7.8	NR or <11.1	<7.8	NR or <11.1	<7.8
Fasting glucose	-	-	-	-	>6.1-6.9	>6.1-6.9	5.6-6.9	>6.1-<7.0	5.6-6.9	>6.1-<7.0
HbA1c	-	-	-	-	-	-	-	5.7-6.4%		
Normal										
*2-h plasma glucose	<6.1	<7.8	<8.0	<7.8	-	<7.8^	-	<7.8^		<7.8^
Fasting glucose	-	<6.4	-	-	-	<6.1	-	<6.1		<6.1

HbA1c glycated haemoglobin
NR- not required
+CS = classic symptoms of polyurea, polydipsea and unexplained weight loss
WHO World Health Organization
ADA American Diabetes Association
† Whole blood glucose concentration otherwise values represent venous plasma glucose
*Venous plasma glucose 2-h after injection of 75g oral glucose load ^Implied
All measures are in mmol/litre excluding HBA1c

1.4.2 Diagnosis and validation in epidemiological studies

The diagnosis of diabetes in epidemiological field surveys is logistically more complex than the diagnosis of diabetes in clinical settings. Additional challenges include the feasibility of carrying out repeated glucose plasma measures on the same population sample (World Health Organization, 2006), processing a large number of blood specimens, and the high cost and inconvenience for both the study participants and the research team (Gavin et al., 1997). In 1997, the ADA recommended that estimates of diabetes incidence and prevalence in epidemiological studies should be made using a FPG test with the diagnostic level set at $\geq$ 7.0mmol/l. This recommendation was based on this test's good reproducibility, its low within-person variability, and its low cost compared to the 'gold standard' OGTT (Gavin et al., 1997).

Although many epidemiological studies have used the FPG test to diagnose both the incidence and prevalence of T2DM (Fox et al., 2007, Aekplakorn et al., 2011, Wang et al., 2009), this diagnostic method has been found to have flaws. Findings from seven Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe studies showed that the prevalence of diabetes diagnosed by the FPG test was much lower than the prevalence found by diagnosing with the 2 hour plasma glucose test (DECODE Study Group and European Diabetes Epidemiology Study Group, 1998). In addition to this, the FPG test has also been criticized for its low sensitivity for diagnosing mild to moderate degrees of impaired glucose tolerance and for its requirement of a long fast that cannot be guaranteed with multiple participants (King and Rewers, 1993).

The WHO has recommended the use of the OGTT, measuring the plasma glucose level 2 hours after a 75-g oral glucose load, for the diagnosis of impaired glucose tolerance and diabetes in epidemiological studies (field studies carried out in non-clinical settings). This recommendation reflects the higher specificity and sensitivity of the 2-hour OGTT when compared to the FPG test (King and Rewers, 1993). For example, the OGTT was more sensitive than the HbA1c test and the FPG test for diagnosing diabetes among Asian Americans (Herman and Zimmet, 2012).

Notwithstanding the wide use of the 2 hour OGTT in epidemiological studies (Ramachandran et al., 2004, Singh et al., 1998, Peng et al., 2000), in recent years both the ADA and the WHO have noted the advantages of using the HbA1c test to diagnose

diabetes (Chen et al., 2012a). This observation applies when haemoglobin dynamics are normal and a certified laboratory A1c test is used (American Diabetes Association, 2013). An A1c diagnosis is convenient for the participant as it does not require a fast, or 2-hour time point for blood collection. As well, the A1c test has low day-to-day variation and diagnostic levels can be set to correspond to detectable retinopathy. However, the A1c test has several problems. Not only is it a more expensive test than the FPG, it may not be feasible in some developing countries due to lack of accessible laboratories that conduct the test using a certified method. Furthermore, epidemiological studies have found that glycation rates may vary by ethnicity. One study found that even when FPG levels were matched, African Americans with and without diabetes had higher HbA1c levels than non-Hispanic whites (American Diabetes Association, 2012). Furthermore, A1c levels increase with age, and as such may be less reliable for diagnosing diabetes in older patients (Huang et al., 2013). A1c levels are also affected by abnormal haemoglobins, high red cell turnover, anemia, and pregnancy (American Diabetes Association, 2012).

Recognizing the limitations of selecting the appropriate diagnostic criteria, recent incidence and prevalence cohort studies of diabetes have used a combination of diagnostic criteria. These have included medication use (Chang et al., 2010), self-reported doctor diagnosis (Maskarinec et al., 2009), and/or hospital records (Okura et al., 2004), as well as the FPG test and OGTT (Wang and Hoy, 2004), and/or HBA1c (Gribble et al., 2012). Evidently the diagnosis of diabetes and glucose intolerance in epidemiological studies is complex and will depend largely on the type of study being conducted, the attributes of the participants involved (e.g. ethnicity, age, pregnancy, hemoglobinopathy, and anemia), and the resources available in the country and area of study. The diagnostic criteria selected will have implications for the incidence and prevalence findings, and for the comparability and validity of these findings (NCD Risk Factor Collaboration, 2016).

1.4.2.1 Self-reported diabetes

Self-report of doctor diagnosis is one of the most common methods used to measure diabetes in observational studies of populations (Rylander et al., 2014, Kurotani et al., 2013, Schneider et al., 2012, Minges et al., 2011). Although self-report is convenient, non-intrusive, and requires fewer resources, its validity and reliability may be in question

(Comino et al., 2013). Issues around the reliability and validity of a self-reported health condition may include the misunderstanding of the questionnaire, lack of formal diagnosis or treatment, an individual's personal characteristics (i.e. age and sex), and/or the type of disease in question (Goto et al., 2013, Okura et al., 2004, Kriegsman et al., 1996).

A few studies have measured the reliability and validity of self-reported diagnosis of diabetes by assessing its level of agreement with other 'gold standards'. These measures have included physical examinations and medical records (Pastorino et al., 2014, Kriegsman et al., 1996, Haapanen et al., 1997), of which medical records have been found to have an agreement with self-report as high as 98% (Manson et al., 1991). Medical records have also been linked, revealing that self-report has 81% sensitivity and 98% specificity for diabetes recorded in patient admission records combined with medical and diagnostic service records)(Comino et al., 2013). Using fasting glucose or medication use as the gold standard, self-report has moderate sensitivity (59-71%) and high specificity (96-97%) for prevalent diabetes and a similar performance for incident diabetes (62-80% sensitivity and 87-89% specificity).

Self-report has also been tested against HbA1c measurement (59-64% sensitivity and 84-87% specificity for incident diabetes) (Schneider et al., 2012), and against fasting glucose or OGTT or HbA1c (70% sensitivity point estimate and 97% specificity point estimate) (Goto et al., 2013). It has also been tested against telephone interview by a study physician and/or using a combination of these measures (Pradhan et al., 2001). Overall, the findings from these studies suggest that self-report detects diabetes with a moderate to high sensitivity and specificity (Schneider et al., 2012, Pastorino et al., 2014). This accuracy of self-report has been attributed to the well-defined diagnostic criteria of diabetes and the requirement for treatment after diagnosis (Margolis et al., 2008, Schneider et al., 2012).

However, these findings may not be generalizable to all study populations. Some of these validation studies were carried out with cohorts that only included women (Manson et al., 1991, Rylander et al., 2014, Pradhan et al., 2001), a specific age range (Comino et al., 2013, Goldman et al., 2003) and/or of specific ethnicity (Odegaard and Pereira, 2013). The few studies that have assessed the validity of self-reported diabetes in Asian

populations suggest that Asian populations may have higher levels of misreporting than Western populations, which may link to traditional cultural beliefs (Goto et al., 2013) Therefore, the validity of self-reported diabetes needs to be assessed in each study population before being used for epidemiological investigations.

1.4.3 Summary – T2DM diagnosis

Diagnosing T2DM is complex and this has been highlighted by the ongoing debate on its appropriate classification and diagnostic criteria over the past five decades. It is expensive in both time and money and infeasible to apply in large populations, and may be subject to measurement error. Diagnosis is even more challenging in large epidemiological studies because some clinical methods for diagnosis are infeasible. Logistically the collection of self-reported health information is a practical and convenient method for detecting disease in large population groups. However, the validity of self-report has been questioned as it has been shown to vary by personal socio-demographic characteristics in different populations. Thus, validation of self-report is required in different populations.

1.5 Trends in the incidence and prevalence of diabetes

1.5.1 Global trends

There have been numerous attempts to estimate the global prevalence of diabetes over the last few decades (International Diabetes Federation, 2015, King et al., 1998, King and Rewers, 1993, McCarty and Zimmet, 1994, Wild et al., 2004, World Health Organization, 2016). In 1993, the WHO Ad Hoc Diabetes Reporting Group provided the first methodologically comparable age-standardized estimates on the prevalence of diabetes. They reported the prevalence of abnormal glucose tolerance for over 150 000 people from 32 countries using data collected between 1976 and 1991. The lowest global prevalence was among populations living traditional lives in developing countries (King and Rewers, 1993). In 1994, estimates on the global burden of diabetes became available and estimated that the total number of people with diabetes ranged between 100 million and 110 million (McCarty and Zimmet, 1994). The estimates made for 1995 were considerably higher and ranged between 118 million (Amos et al., 1997) and 135 million (King et al., 1998). The discrepancy between the two 1995 estimates may be attributed to the different methodologies used between the two studies (Amos et al., 1997, King et al., 1998). Both these studies attributed over 95% of the diabetes burden to T2DM and both predicted that the burden would rise substantially over the next three decades (Amos et al., 1997) (King et al., 1998), reaching 300 million cases by 2025 (King et al., 1998).

An influential source of the global prevalence estimates for diabetes is the International Diabetes Federation (IDF) Diabetes Atlas. Since its first edition in 2000, the estimates have increased from 151 million cases and a 4.6% global prevalence in 2000 (International Diabetes Federation, 2000) to 425 million cases and a 8.8% global prevalence in 2017. The latest IDF Diabetes Atlas projected that the number of affected cases will reach 629 million by 2045 (Figure 1-1); the equivalent of 1 in every 11 adults having diabetes (International Diabetes Federation, 2017).

Although the data collection methodology has varied among the IDF Diabetes Atlas editions, comparisons with national, regional and global data collected by various studies revealed a similar increasing trend in the global prevalence of diabetes (Danaei et al., 2011, World Health Organization, 2016, NCD Risk Factor Collaboration, 2016, International Diabetes Federation, 2017).

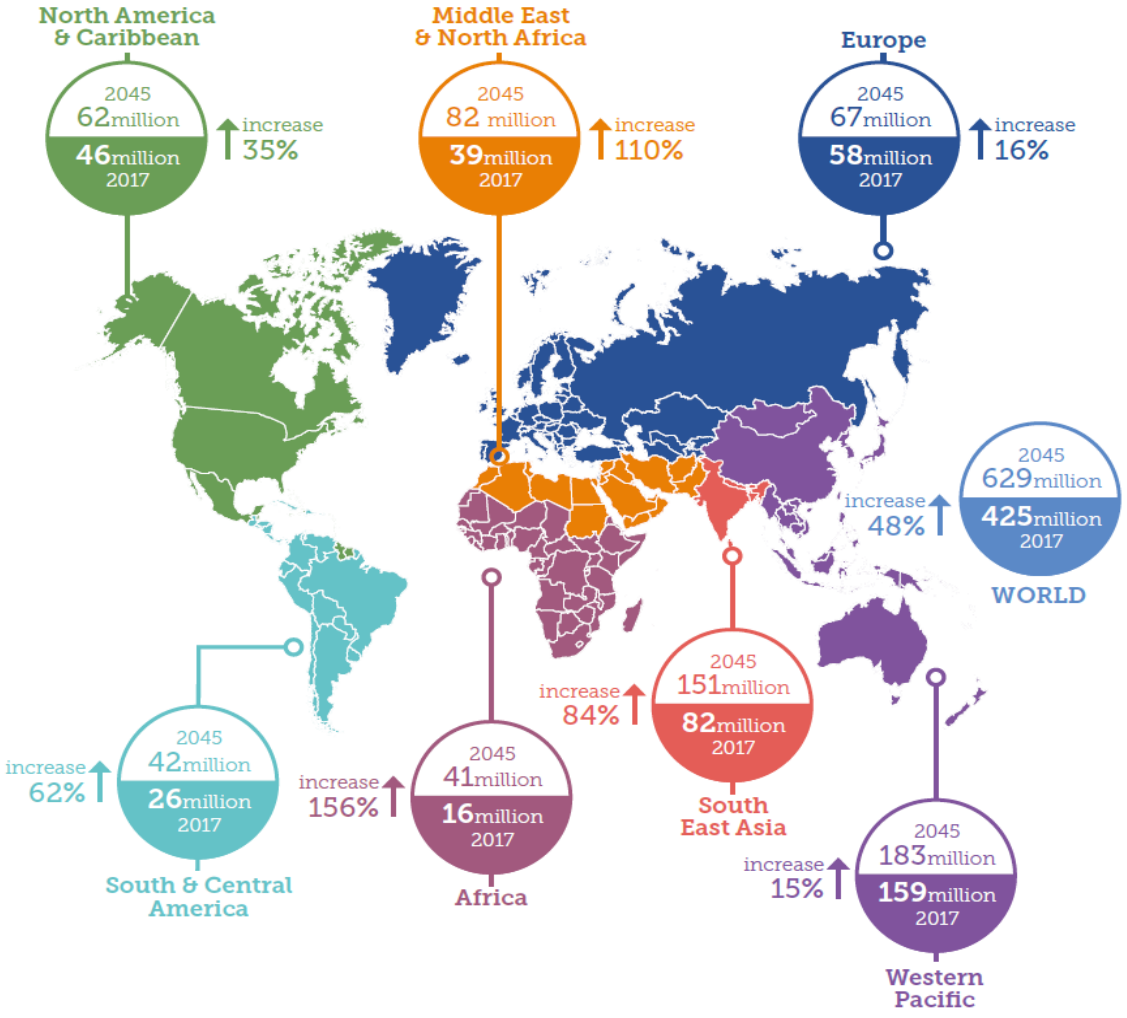


Figure 1-1 Estimated number of people with diabetes globally and by region in 2017 and 2045 (20-79 years) (International Diabetes Federation, 2017)

There are large differences between current estimates (Guariguata et al., 2014, International Diabetes Federation, 2015) and the ones predicted for the same period over a decade ago (Amos et al., 1997, King et al., 1998). The differences arose from methodologic variation and changing diagnostic criteria over the years resulting in higher estimated numbers of diabetes cases after 1997 (Ohlson et al., 1985, Gavin et al., 1997). As well, decreased mortality from diabetes accompanied improving health care systems (Guariguata et al., 2014, Sicree and Shaw, 2007). It is also likely that the increase in estimates over the past two decades is partly attributable to the availability of newer data (Whiting et al., 2011).

Regardless of the different estimations made by different authors, over the past few decades the global prevalence of diabetes has been increasing steadily mostly due to the

increasing incidence and prevalence of T2DM (International Diabetes Federation, 2015). In addition to the existing cases of diabetes, it is likely that current diabetes prevalence underestimates the true prevalence due to a high proportion of the population in both developed and developing countries that has yet to be diagnosed and the use of FPG in many of these surveillance studies, that is likely to underestimate prevalence (Zimmet et al., 2016). Furthermore, by 2040 approximately 532 million adults are predicted to have impaired glucose tolerance, putting them at an increased risk of developing diabetes (International Diabetes Federation, 2017). Thus T2DM is already a global health issue and is expected to increase substantially in the future (Chen et al., 2012a).

1.5.2 Trends in low and middle-income countries

1.5.2.1 Prevalence

The prevalence of diabetes has been rising in both high income and LMICs over the past three decades (Weiguo, 2012). Presently, due to their large populations, LMICs have the highest numbers of people living with diabetes, with approximately 80% of the global population with diabetes living in developing countries (Ramachandran et al., 2010). Furthermore, the prevalence of diabetes is projected to rise predominantly in developing countries in the future (Nolan et al., 2011). This was not always the case. In 1993 the WHO Ad Hoc Diabetes Reporting Group found that the prevalence of diabetes was less than three percent among men and women from a variety of areas including Da Qing in China, rural Bantu homelands and Tanzania in Africa, Chile in South American, southern India and Sri Lanka, and New Caledonia in the Pacific (King and Rewers, 1993). Contrary to these low regional estimates, in 1997 Amos, McCarthy and Zimmet (1997) predicted that due to the large population growth the regions with the greatest increase in diabetes would be Africa and Asia; with Asia predicted to have over 60% of the global diabetic population in 2010. The following year a study by King et al. (King et al., 1998) predicted that the majority of the new diabetes cases between 1995 and 2025 would be diagnosed in developing countries as opposed to developed countries, due to the large growth in the adult population (48% increase in prevalence versus a 27% increase in prevalence); with the largest increases in prevalence expected to occur in China (68% prevalence increase) and India (59% prevalence increase).

A national survey conducted in China supports the early predictions made by Amos, McCarthy and Zimmet (1997) and King et al. (1998). The national study estimated that in 2007-2008 over 92 million adults had diabetes (9.7% of the total Chinese population) and an additional 148 million (15.5% of the total Chinese population) had pre diabetes (Yang et al., 2010) which was higher than the prevalence of diabetes and pre diabetes (2.5% and 3.2%) recorded on a larger sample in 1994 (Pan et al., 1997b). A comparable increase in the prevalence of diabetes was recorded in India by the Chennai Urban Epidemiology Study (CURES) that observed a 72.3% increase in diabetes prevalence between 1989 and 2004 (Mohan et al., 2006, Weiguo, 2012).

Over the past decade, all seven editions of the IDF Diabetes Atlas have consistently found that the largest numbers of diabetes cases globally has been in the IDF's 'western pacific region' (which includes China, Southeast Asia and India). Furthermore, the 7th edition of the Diabetes Atlas predicted that the cases of diabetes in the 'western pacific region' will rise by a further 30% between 2015 (153 million cases) and 2040 (215 million cases), which exceeds the projected 16% increase for Europe (from 60 million in 2015 to 70 million in 2040) and 28% increase for North America and the Caribbean (44 million in 2015 to 60.5 million in 2040) (International Diabetes Federation, 2015). The relatively large number of people with diabetes in this region compared to the rest of the word is mainly attributed to both China and India both having huge populations; and consequently the highest number of people with diabetes (Herman and Zimmet, 2012).

T2DM has emerged at a faster rate in LMICs in Asia than in the western world (Hossain et al., 2007) (Yoon et al., 2006). For instance, over the past 40 years, the prevalence of diabetes in the US doubled from four to eight percent whereas the prevalence of diabetes more than tripled in China between 1980 and 1996, with similar findings reported in Malaysia, Korea and Thailand (Yoon et al., 2006). Between 1982 and 1995, urban Jakarta and Ujung Padang in Indonesia saw an almost four fold increase in the prevalence of diabetes from 1.7% to 5.7% and from 1.5% to 5.4% (Sutanegara and Budhiarta, 2000). Similar increases were observed in Loas, Philippines and Vietnam between 2003 and 2015 (International Diabetes Federation, 2015). Accordingly, LMICs now have the highest prevalence of T2DM globally (Figure 1-2).

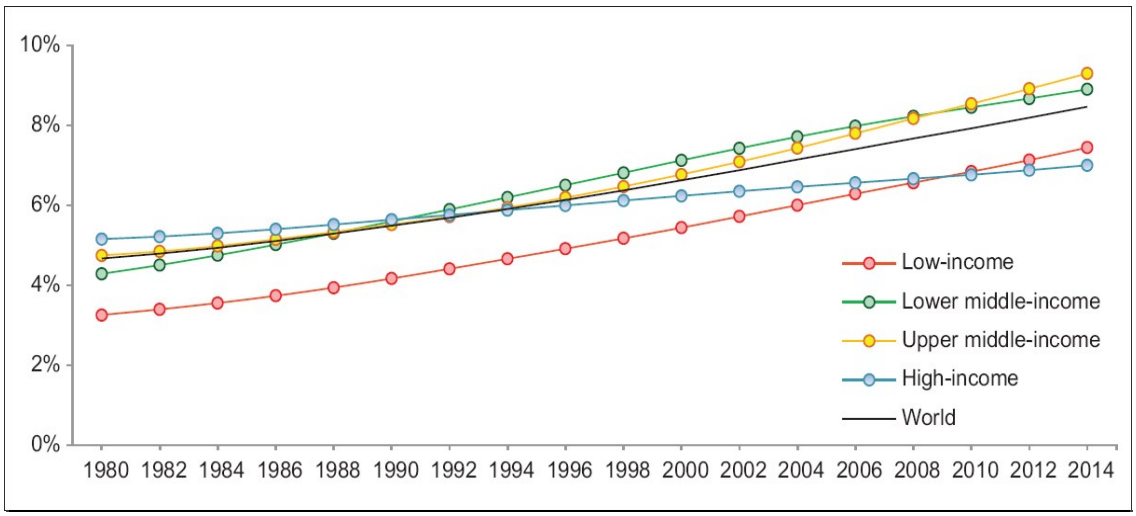


Figure 1-2 Trends in diabetes prevalence by country income group (Roglic, 2016)

1.5.2.2 Incidence

Although incidence rates for T2DM are less documented than prevalence estimates in LMICs, the available data suggest that rates are continuously rising and surpassing those recorded in western populations. The highest T2DM incidence rates have been recorded in Indigenous populations who have been shown to have T2DM rates of over 20.0 per 1,000 person years. These high incidence groups include the Pima Indians (Pavkov et al., 2007), Rural Wanigelas, Nauruans (Dowse, 1996) and the Mauritians (Söderberg et al., 2004). High rates (>10.0 per 1,000 person years) have also been reported for populations living in China (Chen et al., 2012b), Bangladesh (Asghar et al., 2011), and the Philippines (Soria et al., 2009). Although the direct comparison of rates between LMICs and western high-income countries is difficult, due to differences in population age structures and sampling, incidence rates recorded in western countries in North America (Lipscombe and Hux, 2007) and Europe (Bonora et al., 2004) are lower (<10.0 per 1,000 person–years) than those recorded in LMICs.

1.5.3 Trends in Thailand

1.5.3.1 Prevalence

The prevalence of diabetes in Thailand is among the highest in Asia (Chan et al., 2009). According to the Diabetes Association of Thailand, there were 4 million cases of diabetes in 2015 (International Diabetes Federation, 2015). This estimate already surpasses the 2025 estimate of 1,923,000 made by the WHO in 1998 (King et al., 1998). A rising trend

of diabetes prevalence has been observed by successive Thai National Health Examination Surveys NHES over the past two and a half decades (Bureau of Policy and Strategy, 2011). Five NHES were conducted between the years of 1991 and 2014. The national prevalence of diabetes among individuals aged 15 years or over has more than tripled from 2.3% in 1991 to 8.9% in 2014 (Figure 1-3) (Chavasit et al., 2017).

The consistent rise in the recorded prevalence of T2DM in Thailand may be in part attributed to the lower diagnostic criteria (FPG $\geq$7.0mmol/l versus >7.8 mmol/l) used by the three most recent NHES (Aekplakorn et al., 2003, Aekplakorn et al., 2011) or the increase in detection accompanying the implementation of the universal health care coverage and the national diabetes screening campaign in 2002 and 2006 (Prakongsai et al., 2009, Tangcharoensathien et al., 2010). However, despite the implementation of these two programs nearly half of the adults found to have diabetes in the fifth NHES in 2014 had not previously been diagnosed (Aekplakorn et al., 2016). It is also likely that the national prevalence of diabetes may have even been underestimated in the NHES since the diagnosis of diabetes was based solely on a fasting plasma glucose test, which has been found to be less sensitive at detecting diabetes than the oral glucose tolerance test and the HbA1c (Aekplakorn et al., 2003, Aekplakorn et al., 2011). The prevalence of T2DM in Thailand has increased over the past few decades. However, this may partly reflect improved survival or differential testing with those at high risk being more likely to get tested. Incidence data are required to assess the number of new cases of T2DM, to quantify the risk and rate of T2DM in Thailand, and to help estimate the future burden.

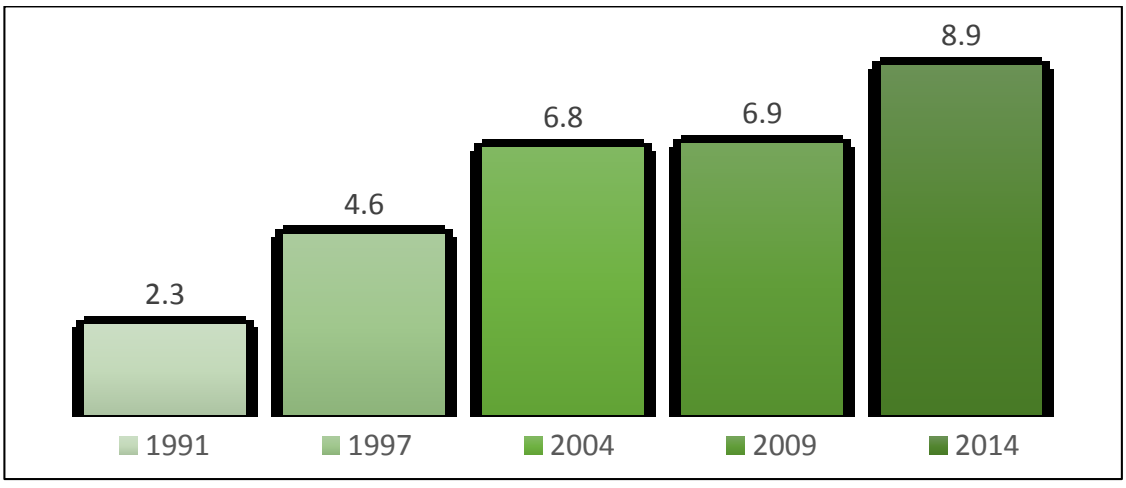


Figure 1-3 Prevalence (%) of diabetes mellitus in Thailand, 1991-2014

1.5.3.2 Incidence

To date, three studies have reported on T2DM incidence in Thailand (Deerochanawong and Ferrario, 2013). The longest of these studies was conducted in employees of a state enterprise involved in the Electric General Authority of Thailand cohort study. This study found that over a 12 year follow-up (1985-1997) the incidence of T2DM was 11.3 per 1000 person-years (Aekplakorn et al., 2006a). The second study was conducted in a group of employees working for government or private agencies in Bangkok. This study found that over a four year follow-up (1999-2003) the incidence of T2DM was 11.4 per 1000 person-years (Jiamjarasrangsi and Aekplakorn, 2005). The third and most recent study was carried out with employees from a university hospital in Bangkok between 2001 and 2005 and found that the incidence rate of T2DM during that time was 13.6 and 6.4 1000 person-years in men and women, respectively, or 7.8 per 1000 person-years combined (Jiamjarasrangsi et al., 2008).

These three studies all provide very useful information about T2DM incidence in professional workers living in Bangkok. However, accuracy of these studies is restricted by sample size (under 7000 participants), occupation, and geographical residence (all participants living within Bangkok). Therefore, the findings from these studies are not generalizable for populations living outside of Bangkok. This creates a knowledge gap regarding the secular trends of T2DM incidence in the national Thai population.

1.5.4 Summary – T2DM epidemiology

The global prevalence of T2DM has increased substantially in recent decades and this growth has occurred predominantly in LMICs. Asia now hosts the majority of the world's population living with diagnosed and undiagnosed diabetes with numbers projected to keep rising as populations continue growing and aging. While the T2DM epidemic is well documented in high income countries in the west, less is known for LMICs in Asia, and this includes Thailand.

1.6 The determinants of type 2 diabetes mellitus

The determinants of T2DM can be classified as either non-modifiable or modifiable (Alberti et al., 2007). In line with the overall aim of this research, this review will focus on the modifiable determinants of T2DM.

1.6.1 Non-modifiable risk factors

1.6.1.1 Genes

Genetics is a strong risk factor for T2DM (Adeghate et al., 2006, Sladek et al., 2007, Langenberg et al., 2011). Over the past 50 years, candidate-gene association studies and family-based linkage studies have been used to assess the causal relationship between genes and T2DM (Maruthur, 2013, Lam and LeRoith, 2012). The family-based linkage studies assessed the association between genes and T2DM by calculating T2DM concordance rates between monozygotic twins and T2DM risk among individuals who had first degree relatives with T2DM. These studies demonstrated that inheritance can increase the risk of T2DM by more than 50% and up to as high as 92% (Nolan et al., 2011, Permutt et al., 2005). Additional evidence of the genetic association with T2DM became available in 2007, when a French case-control study identified the first T2DM susceptibility loci using genome wide association studies (GWAS) (Sladek et al., 2007). Since then, other researchers have found over 40 new loci that have been confirmed among European, Japanese, Indian and various south Asian populations (Agardh et al., 2011a, Nolan et al., 2011).

The risk of T2DM varies by ethnicity, with some ethnic groups sharing specific genetic characteristics that put them at an increased risk of T2DM. Genetics have been used to explain the high prevalence of diabetes recorded among the Pima Indians and Pacific Islanders from Nauru and Fiji (Adeghate et al., 2006). GWAS have found genetic variants associated with T2DM among Asian populations that differ to those found among European populations. One such genetic variant is *FTO*. Although this variant predisposes both European and Asian populations to diabetes due to its effects on obesity, recent evidence suggested that among Asian populations, *FTO*'s effect is not mediated solely through BMI as it appears to be in European populations (Yajnik et al., 2009). It is possible that the increased risk of insulin resistance and T2DM at lower BMIs recorded

frequently among Asian populations may be in part attributed their genetics (Chan et al., 2009).

1.6.1.2 'Thrifty genotype'

Although the evidence supporting the causal relationship between genetic variations and T2DM has strengthened over the past few decades, most researchers argue that the dramatic rise in the global prevalence of T2DM, particularly among some demographic groups, could not be explained by any substantive increase in prevalence of pro-diabetes genetic variations during the short period of the T2DM epidemic (Maruthur, 2013). Rather, some researchers argue that the rising prevalence of T2DM among various ethnic groups can be explained by 'the thrifty genotype hypothesis' (Neel, 1962). According to this hypothesis, during times of famine, genotypes efficient in storing fat were selected as a mechanism for coping with times of food scarcity. Therefore, a genetic variation to store more fat and decrease insulin sensitivity in the muscles would provide an evolutionary benefit for populations living in areas that faced repeated bouts of famine (Maruthur, 2013, Permutt et al., 2005). Based on this theory, it has been suggested that the high prevalence of T2DM recorded among the Pima Indians and other Indigenous populations may be attributed to their genetic predisposition to storing fat caused by their high proportion of thrifty genotypes (Maruthur, 2013, Hu, 2011). Consequently, with the transition from environments that supplied low energy intakes to those that offer an abundance of calories from fat and sugar, their genetic predisposition that would have once served as a protective mechanism would now pose an increased risk for T2DM among these populations (Abate and Chandalia, 2003, Nolan et al., 2011). As such, the thrifty genotype is one theory used to explain why the 'western' diet is associated with a higher risk of T2DM among Asians, Pima Indians and Indigenous populations than among Caucasian and White American populations (Abate and Chandalia, 2003).

1.6.1.3 'Thrifty Phenotype'

There is evidence to suggest that intrauterine malnutrition can cause epigenetic changes that increase the risk of T2DM during adulthood. This phenomenon has been explained by the 'thrifty phenotype hypothesis' (referred to more generally as the 'developmental origins theory' (Barker, 2007). According to this theory, in order to cope with under-nutrition, the foetus must adapt its development. Adaptations include metabolic and

structural changes such as decreased pancreatic β-cell mass, impaired β cell and islets of Langerhans function and increased insulin resistance. Although the thrifty phenotype adaptations are beneficial for the early survival of the foetus, they can increase the risk of T2DM and other chronic diseases later on in life once diet becomes abundant and the impaired β-cells cannot sufficiently regulate insulin (Permutt et al., 2005, Pinney and Simmons, 2010, Hu, 2011). Findings from several studies have indirectly supported this hypothesis and these are considered below.

The National Nutrition and Health Survey in China found that among adults who were exposed to famine in utero, those who consumed western food and traditional foods had a 7.63 and 2.34 odds ratio of hyperglycaemia, respectively compared to unexposed adults (Hu, 2011). Similarly, adults who were restricted to under 800Kcal in utero during the Dutch famine winter period of world war two were found more likely to have impaired glucose tolerance at 50, compared to adults who were in-utero a year before or after the famine (Ravelli et al., 1999). A meta-analysis of 28 populations of different ethnicities reported that a one kilogram (kg) increase in birth weight was associated with a 20% reduction of risk of T2DM (Chen et al., 2012a). As such, it is possible that the dramatic increase in T2DM in developing countries may be partially attributed to the shift from under-nutrition in-utero to the state of over nutrition that has accompanied the growing economies of these countries (Chen et al., 2012a).

1.6.1.4 Gestational Diabetes

Over-nutrition in utero is also associated with the increased risk of T2DM later on in life (Hu, 2011) and is usually attributed to having a mother with diabetes. Maternal diabetes that is specific to pregnancy is called ‘Gestational diabetes’. Gestational diabetes, which is characterized by having glucose intolerance during pregnancy, usually resolves once the mother delivers the baby (Permutt et al., 2005). Although the mother no longer has diabetes once the baby is delivered, the risk of T2DM among the remains increased for the mother and the offspring during adulthood. A higher risk of early onset of T2DM has been recorded among Pima Indians who were born to mothers with gestational diabetes when compared to those born to mothers without gestational diabetes (Misra et al., 2010). Similarly, youth from the multiethnic SEARCH for diabetes youth study who were exposed to gestational diabetes in utero were diagnosed with T2DM at an earlier age than

youth who were not exposed to diabetes in utero (Nolan et al., 2011). Furthermore, an increased incidence rate of diabetes was recorded among siblings born after the mother developed diabetes when compared to siblings born before (Nolan et al., 2011).

1.6.1.5 Age

Together with population growth, the aging of the global population has played a large role in the recent increase in the worldwide prevalence of T2DM (Maruthur, 2013). Aging increases the risk of T2DM through the promotion of age-related muscle mass reduction, and increased visceral fat accumulation (Goodpaster et al., 2003). These physiological changes can lead to increased insulin resistance and consequent β cell dysfunction due to the increased production of insulin secreted to compensate for insulin resistance (Weber et al., 2012). The risk of T2DM exponentially increases with age.

In Caucasian populations, the risk of T2DM increases substantially from an age of ~65. This is different to Asian populations exhibiting increased T2DM risk from a younger age of ~45 (International Diabetes Federation, 2015). The age-T2DM association has been found to be modified by ethnicity, with Asian populations demonstrating higher postprandial glycaemia and insulinemia when matched with Caucasian populations (Decode-Decoda Study Group and European Diabetes Epidemiology Group, 2003). Asians may experience shorter latency to T2DM development, resulting in the development of T2DM at younger ages than Caucasian populations (Weber et al., 2012).

1.6.2 Modifiable risk factors

1.6.2.1 Obesity

Overweight and obesity are well-established risk factors for T2DM (Hossain et al., 2007, Chen et al., 2012a, Permutt et al., 2005). Adiposity increases T2DM risk by secreting hormones and adipokines from adipose cells that increase insulin resistance (Bray, 2004). The risk of T2DM substantially increases as adiposity increases. This gradient has been found to be stronger in Asian populations with risk increasing at ranges of BMI considered to be in the ‘healthy’ weight range in Caucasian populations.

A likely explanation for this increased risk of T2DM in Asians is body composition. Unlike Caucasian populations who are prone to storing fat in their subcutaneous fat depots, Asian populations are prone to accumulating fat in their visceral cavity (Tchernof and

Després, 2013). T2DM risk increases with central distribution of body fat, and in particular, with visceral adiposity (Carey et al., 1997, Wang et al., 2005). Visceral fat is more likely to release free fatty acids that can be up taken and stored in the muscle, pancreas, and liver than general adiposity and has a stronger association with insulin resistance and T2DM risk (Snijder et al., 2006). Accordingly, the higher propensity to visceral adiposity in Asian populations may in part explain the higher rates of T2DM in LMICs in Asia.

Overweight and obesity, and their relevant BMI cut-points associated with T2DM risk, have been well validated in Caucasian populations. However, the appropriateness of these BMI cut-points for Asian populations is less clear. In 2000, the WHO recommended that lower Asian-specific BMI-cut points may be necessary for defining overweight (23-<25kg/m^2) and obesity ($\geq$25kg/m^2) in Asian adults based on T2DM and cardiovascular disease risk prevalence studies available at the time. In 2004, the WHO put out an additional statement concluding that due to the lack of consistent data, the Asian specific BMI-cut points for defining T2DM and cardiovascular disease risk are unclear (World Health Organization Expert Consultation, 2004). Since then few longitudinal studies have assessed the validity of lower BMI cut-points in Asian populations and this includes Southeast Asian populations. Accordingly, T2DM and body size relations in Southeast Asian adults need further research.

1.6.2.2 Physical Activity and sedentary behaviour

Physical activity (PA) is assocatied with the reduced risk of T2DM. It does this both indirectly and directly. Indirectly, PA reduces the risk of T2DM by shifting the balance between energy intake and energy expenditure, through its prevention of weight gain. Directly, PA can improve insulin sensitivity by increasing muscle mass and subsequently the porportion of insulin sensitive muscle fibers (van Dam, 2003). There is vast evidence to support the inverse association between PA and T2DM risk (van Dam, 2003, World Health Organization, 2011a, Pan et al., 1997a, Diabetes Prevention Program Research Group, 2002). One lifestyle intervention study that ran for almost 3 years found that conducting at least 150 minutes of moderate PA each week has been found to reduce the risk of diabetes by 27% (Diabetes Prevention Program Research Group, 2002). A recent

review study found that cohort studies from the US, Australia and the Netherlands have also found similar associations between PA and reduced risk of diabetes (van Dam, 2003).

Sedentary behaviour increases the risk of T2DM. One US study observed that men who watched over 40 hours of television per week were 187% more likely to develop T2DM than men who only watched 0-1 hour of tv per week (Hu et al., 2001). In one group of women, a 2 hours a day increase in television watching was associated with a 14% increase in the risk of diabetes (Hu et al., 2003). Furthermore, another study found that the T2DM incidence rate was 1.86 for women who watched ≥5 hours of television per day compared with 1.0 for women who watched less <1 hour of television per day, independent of physical activity (Krishnan et al., 2009).

1.6.2.3 Diet

Dietary intake has a key role in the control of blood sugar and can affect both insulin sensitivity and insulin release within three days of its modification, an effect that is too rapid to be attributed to obesity (Kahn et al., 2006). The effect of diet on T2DM risk is complex and may be determined by the nutrient, food, or diet in question. Diet is a major determinant of T2DM both dependently and independently of obesity (Odegaard and Pereira, 2013).

1.6.2.3.1 Carbohydrates

Carbohydrates are major determinants of blood sugar and therefore can play a critical role in the development of T2DM (de Koning et al., 2013). Carbohydrates, named for their makeup of carbon, hydrogen and oxygen, are one of the three major macro-nutrients consumed for food energy. They can be categorized into two major types; simple and complex. Simple carbohydrates can be further subcategorized into monosaccharides and disaccharides (for example glucose, fructose and sucrose). Complex carbohydrates can be further subcategorized into oligosaccharides and polysaccharides (for examples starch and dietary fiber) (de Koning et al., 2013).

Simple and complex carbohydrates have different effects on T2DM risk. Some complex carbohydrates such as whole grains and fibers have been associated with decreasing the risk of T2DM (Hu, 2011, Salas-Salvadó et al., 2011); others, including white rice and

potato, have increased the risk of T2DM just as much as simple carbohydrates. Thus, although carbohydrates, both simple and complex, are associated with T2DM risk, the nature of their effect is determined by the 'quality' of the carbohydrate (Salas-Salvadó et al., 2011).

One measure used to determine the 'quality' of carbohydrates is the glycaemic index (GI). The GI, originally developed in 1981 to improve the management of type 1 diabetes, is a ranking system that categorizes foods based on their postprandial glucose-raising effect. The index is scored between 0 and 100. To categorize a carbohydrate using the GI, 50 grams of the carbohydrate are consumed and compared with a reference carbohydrate that has a GI of 100, such as glucose or white bread. Subsequently, the Glycaemic Load (GL), which helps to reflect the carbohydrate quality and quantity, can be calculated by multiplying the GI of the carbohydrate by the serving size (Salas-Salvadó et al., 2011, Salmeron et al., 1997). Foods are considered as "high GI" if their index is over 70 and "low GI" if they have GI of less than 55 (Atkinson et al., 2008). High GI foods include sugar-sweetened beverages (SSB), white potatoes and candies. Low GI foods include pulses such as lentils, whole grain products such as rye and wholemeal bread, as well as various vegetables (de Koning et al., 2013).

High GI/GL diets produce high levels of blood glucose, which require a large secretion of insulin. Over extended periods, the continual elevated frequency of insulin secretion required to cope with the rapidly absorbable carbohydrates may lead to oxidative stress of the pancreatic β cells. This can lead to the dysfunction and failure of these cells to secrete insulin and eventually T2DM (Hu, 2011, Goran et al., 2013).

Another way that high GI/GL carbohydrates may increase the risk of T2DM is through lipotoxicity (high free fatty acid (FFA) concentrations). A few hours after the consumption of high GI carbohydrates, a counter regulatory hormone response is triggered to restore euglycemia, which stimulates the glycogenolytic and gluconeogenic pathways. These pathways elevate FFA concentrations. As a result of elevated FFA concentrations, there is a down-regulation of insulin-mediated glucose uptake, thereby increasing insulin resistance (Halton et al., 2006, de Koning et al., 2013).

1.6.2.3.2 Fat

The consumption of dietary fat has been found to play a role in the aetiology of T2DM (Odegaard, 2013). Dietary fat is also one of the three major macro nutrients consumed for food energy and contains more than double the kilocalories (Kcals) per gram than carbohydrates and proteins. Dietary fat can be further broken down into its four major fatty acid classes. These include saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA) and trans-fatty acids (TFA). Although all foods that contain dietary fat will have a mixture of SFA, MUFA and PUFA, the proportions of these fatty acids (FA) will differ by food; with animal sources containing a higher proportion of SFAs and plant fat sources and fish and oils containing higher proportions of MUFA and PUFA (Odegaard, 2013).

A high fat diet has been associated with both an increased risk of T2DM (Abate and Chandalia, 2003) and a reduced risk of T2DM (Salas-Salvadó et al., 2011, Meyer et al., 2001) and it appears that the effect of dietary fat on the development of T2DM depends on FA composition of the food (Salas-Salvadó et al., 2011, World Health Organization, 2011a). One mechanism whereby the different classes of FA may affect the risk of T2DM differently is through their role in the cell membrane. The cell membrane is comprised of phospholipids that are made up of FA. The types and ratio of FA consumed can alter the physicochemical property of cell membranes, subsequently altering the function of the cell membrane. Therefore, a higher proportion of SFA than PUFA in the cell membrane may reduce the membrane's permeability and glucose transport function; thereby leading to high blood glucose and insulin resistance (Ginsberg et al., 1981). A different mechanism whereby FAs may affect T2DM risk may be through gene expression. In vitro cell studies have shown that some FA, particularly PUFA, can improve insulin sensitivity by inhibiting hepatic lipogenesis and upregulating hepatic FA oxidation (Odegaard, 2013).

Various case-control studies and cohort studies have found that high intakes of SFAs and TFAs were associated with an increased risk of T2DM (Chan et al., 2009, Bulló et al., 2007, Salas-Salvadó et al., 2011) and that MUFAs and PUFAs were associated with a reduced risk of T2DM (Meyer et al., 2001). However some of these results have been inconsistent (van Dam, 2003, Odegaard, 2013) and likely to be confounded by the

complex nature of assessing dietary fat intake and the lifestyle and food sources associated with it (Salas-Salvadó et al., 2011, Meyer et al., 2001).

1.6.2.3.3 Protein

Findings from various prospective studies have indicated that dietary protein intake is associated with T2DM risk (Salas-Salvadó et al., 2011, Ericson et al., 2013, Odegaard and Pereira, 2013). Dietary protein, the third major macronutrient consumed for energy, is made up of 20 amino acids and is present in both animal sources (i.e meat, dairy and eggs) and plant sources (i.e. legumes, soy products and beans) (Song and Lui, 2013). How protein intake affects the risk of T2DM may be influenced by the source of the protein as well as the duration and level of intake. Evidence from prospective studies suggests that protein from animal source foods increases the risk of T2DM (Sluijs et al., 2010, Duc Son et al., 2005, Ericson et al., 2013) whereas intake of protein from plant source foods was associated with a decreased risk of T2DM (Villegas et al., 2008, de Koning et al., 2011a). Short term ($\leq$6 months) high protein intakes have been associated with stimulating insulin secretion, preventing weight gain and reducing carbohydrate intake, which can improve glycaemic control thereby reducing T2DM risk (Promintzer and Krebs, 2006). Conversely, long term ($\geq$6 months) high protein intakes have been associated with increasing insulin resistance and fasting plasma glucose, thereby increasing T2DM risk (Linn et al., 2000). One mechanism that may explain these different effects is the difference in the amino acid profile of animal and plant source proteins. Certain amino acids may increase insulin secretion and/or glucagon concentration (i.e. arginine) (Gannon et al., 2002), while others (i.e. histidine) do not (Floyd Jr et al., 1966). The amino acid profile of animal source proteins and plant source protein are different, therefore this may play a role in the different T2DM risks associated with animal and plant source proteins (Song and Lui, 2013). Similarly, this may explain the difference in risk among the different animal sources of protein. For instance, fish, which has been associated with a reduced risk of T2DM, has a different amino acid profile to red meat that has been associated with an increased risk of T2DM (Soucy and LeBlanc, 1999). Other mechanisms may explain the association between plant source proteins and reduced risk of T2DM such as the effects of other compounds found in these foods (i.e. the flavonoid content or phytoestrogens found in soy products), however this requires further investigation (Mueller et al., 2012).

1.6.2.3.4 Beverages

Recent evidence suggests that there are a group of beverages with added sugar (Xi et al., 2014, Malik et al., 2010) and without added sugar (De Koning et al., 2011b, Huxley et al., 2009, Salas-Salvadó et al., 2011) that are associated with T2DM risk

1.6.2.3.5 Sugar-sweetened beverages

Findings from a group of cohort studies suggest that daily consumption of sugar sweetened beverages (SSB) increases the risk of developing T2DM by between 22% (Romaguera et al., 2013) and 83% (Schulze et al., 2004). Evidence from a cohort of nurses in the US suggests that BMI might mediate about 50% of this effect (Schulze et al., 2004). Cohort studies conducted in other countries found that after adjusting for BMI, the risk of T2DM associated with daily SSB intake varied between 18% (Romaguera et al., 2013) and 67% (Odegaard et al., 2010, Montonen et al., 2007) with one study losing statistical association after adjusting for BMI (Palmer et al., 2008). The majority of these studies have been carried out with Caucasian or African populations (Montonen et al., 2007, Palmer et al., 2008, De Koning et al., 2011b).

The three available studies carried out in Asian populations had conflicting results (Sakurai et al., 2014, Odegaard et al., 2010). While it is possible that age and sex differences between study cohorts may explain some of these differences, it remains unclear whether SSB intake is associated with increased risk of T2DM among Asians who have lower BMI levels and/or whether this association is primarily mediated through BMI or weight gain. Further research is required to understand the contribution of SSB intake to T2DM risk among Asian populations.

1.6.2.3.6 Milk

High milk consumption versus low milk consumption has been found to be associated with a reduced risk of T2DM (Liu et al., 2006, Choi et al., 2005, Tong et al., 2011). This inverse relationship has been mostly attributed to the low fat variety, thought to be attributed to the lower levels of SFAs and TFAs found present in low fat milk (Salas-Salvadó et al., 2011). It has been suggested that the inverse relationship between high milk consumption and reduced risk of T2DM may be in part attributed to the calcium found in the milk since low calcium intakes has been found to be associated with a higher T2DM risk (Pittas et al., 2007). However, a recent study adjusted for calcium intake and

this did not affect the association between milk intake and T2DM (Grantham et al., 2013). Further research is required to understand the milk and T2DM association.

1.6.2.3.7 Artificially sweetened beverages

The association between artificially sweetened beverages (ASB) and T2DM has been assessed by a few recent cohort studies (De Koning et al., 2011b, Nettleton et al., 2009, Palmer et al., 2008). Although some studies have found that ASB intake increased the risk of T2DM (De Koning et al., 2011b, Nettleton et al., 2009), these results may reflect reverse causation, i.e. the obese and diabetic participants in these studies may have been aware of the weight gain associated with SSB consumption and therefore switched to ASBs (Hu and Malik, 2010). Therefore, based on the current evidence causality between ASBs intake and T2DM cannot be established.

1.6.2.3.8 Alcohol

Alcohol has been found to increase or decrease the risk of T2DM depending on the quantities and frequencies of intake (Hu, 2011). Evidence from two meta-analyses that reviewed 35 cohort studies between them indicated that alcohol consumption has a J-shaped association with T2DM incidence. These studies found that light-to-moderate alcohol consumption (22/day for men and 24g/day for women, or 1-2 drinks per day) was associated with a 30-40% reduction in the risk of T2DM when compared to no alcohol intake (<6g/day) or heavy alcohol consumption (consumption of more than 3 drinks per day or >50g/day for women and >60g/day for men) (Baliunas et al., 2009); with a similar increased risk of T2DM observed among lifetime abstainers and heavy alcoholic drinkers (Koppes et al., 2005). Light-to-moderate alcohol intake may have anti-inflammatory effects and may increase HDL cholesterol offering potential explanations for the observed risk reduction. The deleterious effects of heavy alcohol consumption may be attributed to excess caloric intake which can lead to obesity, disturbance of carbohydrate metabolism and pancreatitis, which can contribute to development of diabetes (Hu, 2011, Greenaway, 2012). Recent evidence from a large Danish cohort suggests that the effects of alcohol on T2DM may also depend on the type of alcohol beverage consumed (Holst et al., 2017). However, further research is needed to confirm these findings

1.6.2.3.9 Dietary Patterns

Assessing the relationship between single nutrients or foods and disease risk is complex as the compounds in the foods can interact, be correlated with one another and/or the effects of a single nutrient may be too small to be picked up in a study (Esposito et al., 2010). Moreover, specific foods and nutrients are rarely consumed independently of other nutrients (Odegaard, 2013). Recognizing this, several recent studies have assessed the effect of diet on T2DM risk by assessing the relationship between specific dietary patterns and T2DM incidence. However, most of these studies were conducted in developed high income countries (van Dam et al., 2002, Hodge et al., 2007, Bauer et al., 2013, Schoenaker et al., 2013).

In these studies, the dietary pattern that has consistently been associated with an increased risk of T2DM incidence has been characterized by the high consumption of red meat, processed and low fiber foods, SSBs, and starchy foods and has been referred to as the 'western diet' (Mayén et al., 2016). Conversely, the dietary pattern that has consistently been reported to reduce the risk of T2DM incidence has been characterized by the high consumption of fruits and vegetables, whole grains, fish and poultry and referred to as the 'prudent' 'conservative', or 'healthy diet' and/or the 'Mediterranean diet' when olive oil and wine are consumed along with a healthy diet (van Dam et al., 2002, Hodge et al., 2007, Bauer et al., 2013, Schoenaker et al., 2013, Esposito et al., 2010). A review of ten large prospective cohort studies that followed more than 190 000 individuals for between two and twenty three years found that a 'healthy' diet was responsible for between a 15% and 83% reduction of risk of T2DM (Esposito et al., 2010). Similarly, a meta-analysis that included six studies that assessed fruit and vegetable intake found that consuming 1.35 servings of green leafy vegetables per day compared to 0.2 servings per day was associated with an estimated 14% reduction in the risk of T2DM (with 1 serving equivalent to 106 g)(Carter et al., 2010).

The negative effect of the 'western diet' on T2DM risk may be attributed to chronic inflammation. Results from different studies have indicated that a western diet was strongly related to markers of inflammation including C-reactive protein, interleukin-6, intracellularadhesion molecule-1, vascular, cell adhesion molecule-1, and E-selectin, which have been previously associated with increased risk of T2DM (Esposito et al., 2010,

Salas-Salvadó et al., 2011, Koppes et al., 2005). Conversely the protective effects of the 'prudent' or 'Mediterranean' diet on T2DM risk may be attributed to the high levels of antioxidants found in this diet such as the vitamin C in the vegetables and the polyphenols in the wine (Esposito et al., 2010).

1.6.2.4 Smoking

In a recent meta-analysis of 25 studies, smoking was associated with a 44% increased risk of T2DM (Willi et al., 2007). Smoking increases the risk of diabetes by reducing insulin secretion responses, which lead to insulin resistance (Chan et al., 2009). Furthermore, due to its anti-estrogenic effects, smoking may also cause hormonal imbalances that may lead to increased obesity; however this mechanism needs further investigation.

1.6.2.5 Education and income

Evidence suggests that the association between education, income and T2DM risk may depend on a country's stage of economic development (Figure 1-4). Studies from high-income countries have shown an inverse relationship between education and income, or socio-economic position (SEP), and T2DM risk (Agardh et al., 2011b) suggesting that SEP inequalities may associate with increased T2DM risk (Sommer et al., 2015). Conversely, in studies from LMICs, SEP has been shown to have a positive association with T2DM until a country reaches advanced stages of economic development (equivalent to a gross national product (GNP) per capita of ~US $2500) (Monteiro et al., 2004). At this stage of economic development, the risk of T2DM begins to rise predominantly in the low SEP group. These findings suggest that the SEP-T2DM association is complex and may differ between economies (Jones-Smith et al., 2012). However, longitudinal data from LMICs at different stages of economic development are required to confirm this.

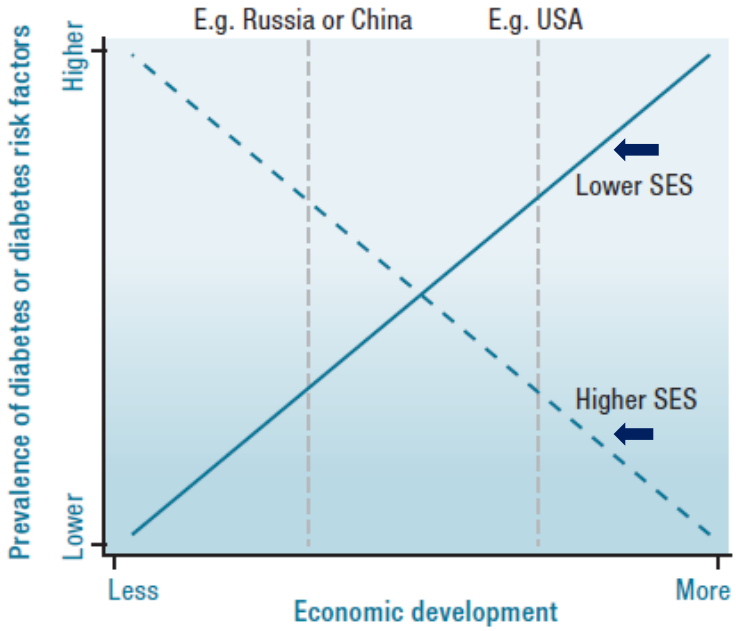


Figure 1-4 Changing associations between economic development, socioeconomic status (SES) and prevalence of diabetes or diabetes risk factors adapted from (Blas and Kurup, 2010)

1.6.2.6 Urbanization

Like education and income, the association between area of residence and T2DM may also depend on a country's level of economic development (Figure 1-5) (Maruthur, 2013, Lam and LeRoith, 2012). In HICs in the west, living in a rural area of residence has been associated with an increased risk of T2DM. This association may be explained by lower SEP, reduced access to fresh foods, and the dearth of health care services available in rural areas (Blas and Kurup, 2010). Conversely, a higher prevalence of T2DM has been observed in urban areas in many LMICs (International Diabetes Federation, 2015). This urbanization effect on T2DM is thought to be mediated through the increased availability of highly processed foods (Banwell et al., 2013), increased sedentary behaviour associated with higher incomes, purchase of labour saving devices, (Ramachandran et al., 2010, Lam and LeRoith, 2012, Sicree and Shaw, 2007), increased likelihood of surviving to a later age as food becomes safer and more accessible, and less manual work (Maruthur, 2013).

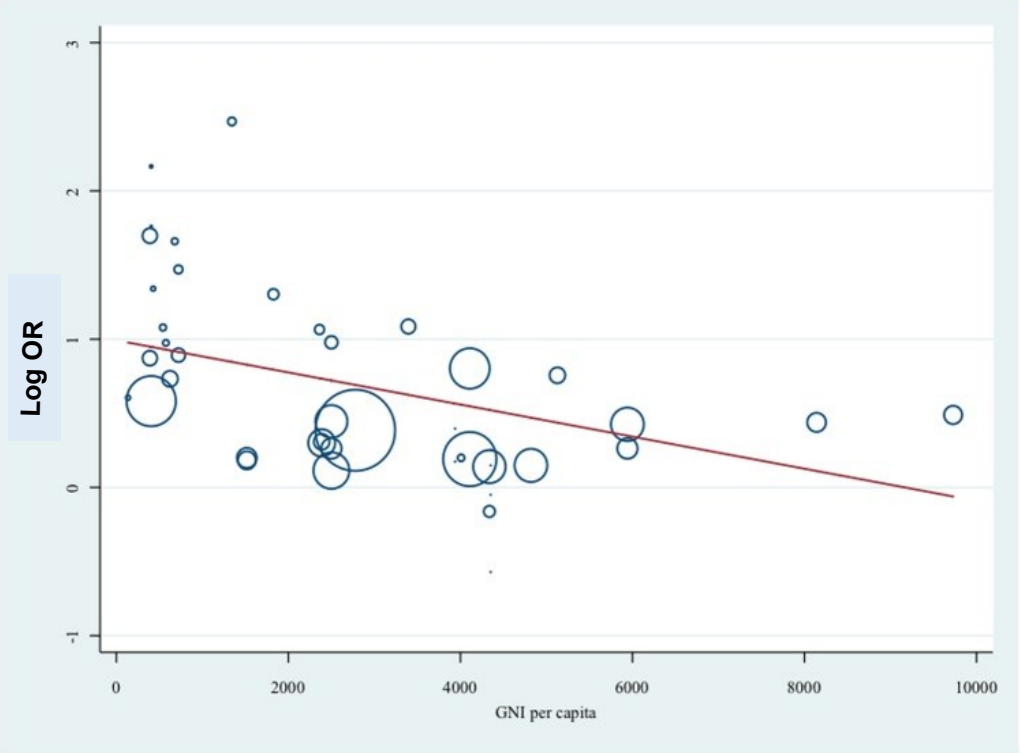


Figure 1-5 Association (log odds ratio) between living in an urban environment and obesity by gross national income per capita in US dollars

Size of circles reflects sample size. Higher log odds ratio reflect larger effect size for living in an urban environment and obesity compared with rural residence (Angkurawaranon et al., 2014).

Recent studies from LMICs have shown that as a country progresses along the epidemiological transition and becomes more economically stable, the association between urbanization and T2DM begins to resemble that noted in HICs. Indeed, in the largest nationwide population-based study of adults conducted in India, both extremes were found. Urban residents in relatively wealthy areas with low SEP had more T2DM. Meanwhile, in poor rural areas, residents with high SEP had more T2DM (Anjana et al., 2017). Similar findings were noted in China, where high SEP rural residents were found to have diabetes rates similar to those reported in urban residents a decade earlier (Fu et al., 2011). In Thailand, more undiagnosed diabetes has been noted in men from rural areas compared to those from urban areas (Aekplakorn et al., 2011). These findings suggest that in the near future, the prevalence of diabetes in upper-middle income countries will be the highest in high SEP rural and low SEP urban individuals. However, longitudinal data are required to confirm these findings.

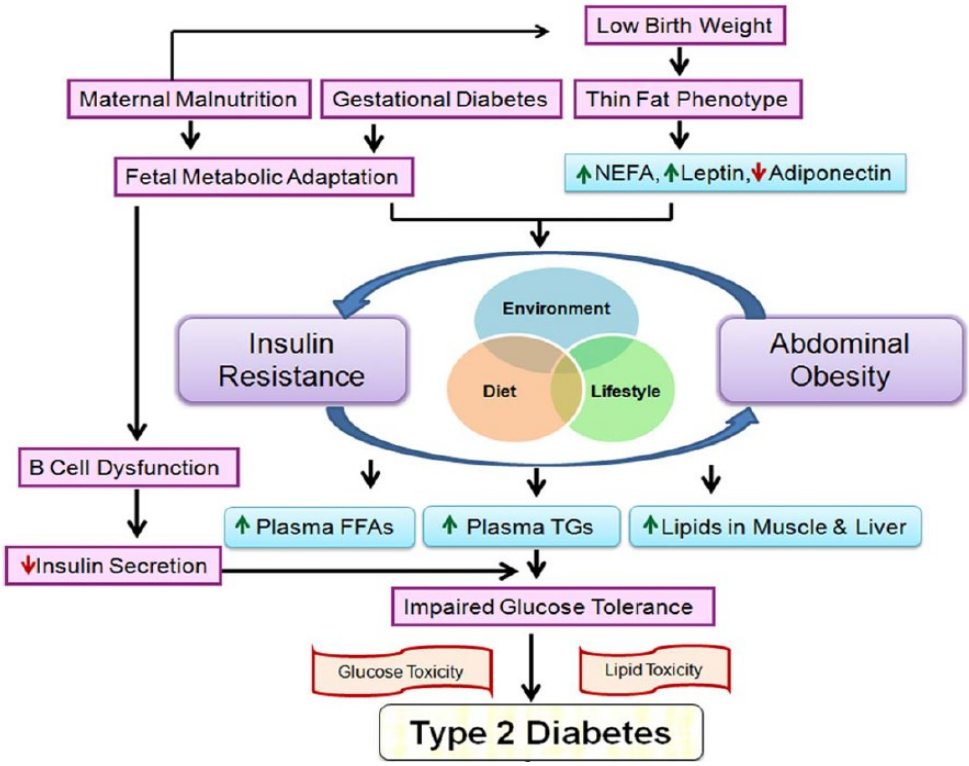


Figure 1-6 Pathophysiological pathways and environmental drivers contributing to type 2 diabetes (Pandey et al., 2015)

1.6.3 Summary – determinants of T2DM

Many risk factors for the diabetes epidemic in western HICs are now well known. These include age, genetics, obesity, health-risk behaviours (e.g. diet, smoking and sedentariness), and certain environmental and socio-demographic attributes like area of residence and SEP (Figure 1-6). In LMICs, less information is available and most derives from cross-sectional studies. The available LMIC literature suggests that T2DM risk factors may depend on country-specific dynamics and ethnicity. Longitudinal data are required to identify the local risk factors driving T2DM in LMICs, including Southeast Asia. This lack of epidemiological information includes Thailand and it has been actively investigating emerging non-communicable diseases including T2DM.

1.7 Transitions

The great transformations affecting the health state of populations in HICs noted over the last century have been explained as components of coherent population transitions that in some way connect to the improved environment, nutrition, and health. Several transitional

models will be reviewed to help explain the recent rise in T2DM across LMICs in Asia. These include the demographic and epidemiological transitions, the health transition, the nutrition transition, and the health-risk transition.

1.7.1 Demographic and epidemiological transitions

The demographic transition refers to a population transition from high fertility and mortality to low fertility and mortality that occurs in all countries as they 'modernize' from a pre-industrial society to an urban industrialized society (Kirk, 1996). This theory attempts to explain how changes in family size and age structure of populations inevitably accompany historical falls in mortality and fertility patterns. To explain the cause of mortality decline that initiates the demographic transition, Abdel Omran developed the epidemiological transition theory, which describes changes in health and disease patterns (1971). His theory proposes that the shift from high to low mortality relates to the shift from infectious diseases towards lifestyle, degenerative diseases as the principle causes of death (Omran, 1971). Omran proposed three successive stages of the epidemiological transition:

1) "The age of pestilence and famine"-characterized by high mortality rate and low life expectancy due to high rate of infectious diseases

2) "The age of receding pandemics"- characterized by a steady decrease in mortality and increased life expectancy due to a decrease in infectious diseases

3) "The age of degenerative and man-made diseases"- characterized by a continual decline in mortality, increased life expectancy, due to the degenerative diseases (i.e. diabetes) becoming the main causes of death.

Omran described three distinct models of the epidemiological transition based on the onset of the transition, its speed of occurrence, and the country's state of modernization and transition from high to low mortality. In the first model 'the classical model', the transition happens over a long period of time, as noted in western countries like England. In the second model 'the accelerated model', the transition occurs over a shorter period of time, as noted in Japan. In the third model, 'the contemporary or delayed model', the

transition has begun but is not yet completed, as noted in certain developing LMICs that are undergoing rapid economic growth where fertility still remains high (Omran, 2005).

1.7.2 Health transition

Like the Epidemiological transition, the Health Transition also describes the changes in disease patterns that occur alongside economic development, but it also considers the social, cultural, and behavioural determinants that drive this transition in health outcomes. Some of the determinants considered in this theory include: the 'health care transition', which refers to the change in health-service response to health conditions (Frenk et al., 1989), increasing maternal education, the uptake of 'western' cultural ideals, the position of women in society and the family, especially when making scientific decisions about health care, and disease (Caldwell, 1993).

1.7.3 Nutrition transition

The nutrition transition occurs alongside the demographic, epidemiological and health transitions. This theory describes the large shifts in diet, physical activity, nutritional status and lifestyle nutritional diseases that accompany a country's socioeconomic development. The nutrition transition is made up of 5 patterns (Popkin, 1993, Popkin, 1994). The first two patterns (*collecting food* and *famine*) describe a hunter-gatherer existence where food shortage is high, diet variety is low, and nutritional deficiencies are the main nutritional outcome. This pattern is commonly seen in low-income countries. In the third pattern (*receding famine*), income growth leads to an increased consumption of fruit, vegetables, and protein, receding famine and increased time leisure activity due to the availability of labour saving devices. The fourth pattern (degenerative diseases) is similar to the third stage of the Epidemiological transition (*the age of degenerative and man-made diseases*). In this pattern, diets converge from 'traditional' (high in fibre and fruit) to 'western' (high in fat, added sugar, and meat), physical activity is reduced, and degenerative-lifestyle nutritional diseases like obesity and T2DM emerge. This pattern arises as countries progress from low to middle income economies. The shift in behaviours and health outcomes in pattern four are driven by increased urbanization, changing food systems, and globalization of multinational supermarkets (Popkin et al., 2012, Kelly et al., 2014). In the fifth and final pattern (*behavioural change*) health promotion is increased. Diets shift towards increased fruit and vegetable intake and

reduced animal product consumption, physical activity is increased and degenerative diseases are reversed or delayed. This pattern mostly occurs when countries progress to high-middle income or high-income economies, as noted in Japan and Australia (Popkin, 2006).

1.7.4 Health-Risk transition

The Health-risk transition theory incorporates the various transitional theories (e.g. demographic, epidemiological, health, and nutrition). In addition to these components, it also describes the transformation of family structures, work place settings, health-risks (environmental, societal and behavioural) and related outcomes (attitudes, understandings of health, culture, and disease) that accompany a country's socioeconomic development.

1.7.5 Transitional Thailand

Thailand is a Southeast Asian country that has experienced rapid economic growth in recent decades. This growth has induced changes in health-risks (environment and behaviour) and a demographic, epidemiological, health, and nutrition transition, which combined to produce a powerful health-risk transition.

1.7.5.1 Economic growth and urbanization

Thailand has achieved substantial economic growth since the late 1950's. Between 1968 and 1986 Thailand had an annual average GNP growth rate of 6.7%. The following decade (1987-1996), Thailand had one of the fastest growing economies across Asia (Warr, 2007). This rise was halted between the years of 1997 and 1999 but boomed again in 2003 (Warr, 2007). Alongside this economic growth, the national poverty level halved from 21.9% in 2006 to 10.5% in 2014 (The World Bank, 2016) and the proportion of Thailand's urban population more than doubled from 20% in 1960 to 50% in 2015 (The World Bank, 2016).

1.7.5.2 Demographic and epidemiological transition

Thailand's demographic transition has been evidenced by major increases in life expectancy, a growing aged population, and decreased fertility and childhood mortality (Figure 1-7). In 1960, the life expectancy was estimated to be 55. By 2014 this had increased to 74. This increase shifted the age distribution of the population. Accordingly, the proportion of Thai adults aged over 65 years tripled from three percent in 1960 to 10%

in 2015 (The World Bank, 2016). In parallel, the total fertility rate decreased from 6.1 in 1960 to 1.5 in 2014 and infant mortality fell from 102 to 10.5 per 1000 live births between 1960 and 2015 (The World Bank, 2016).

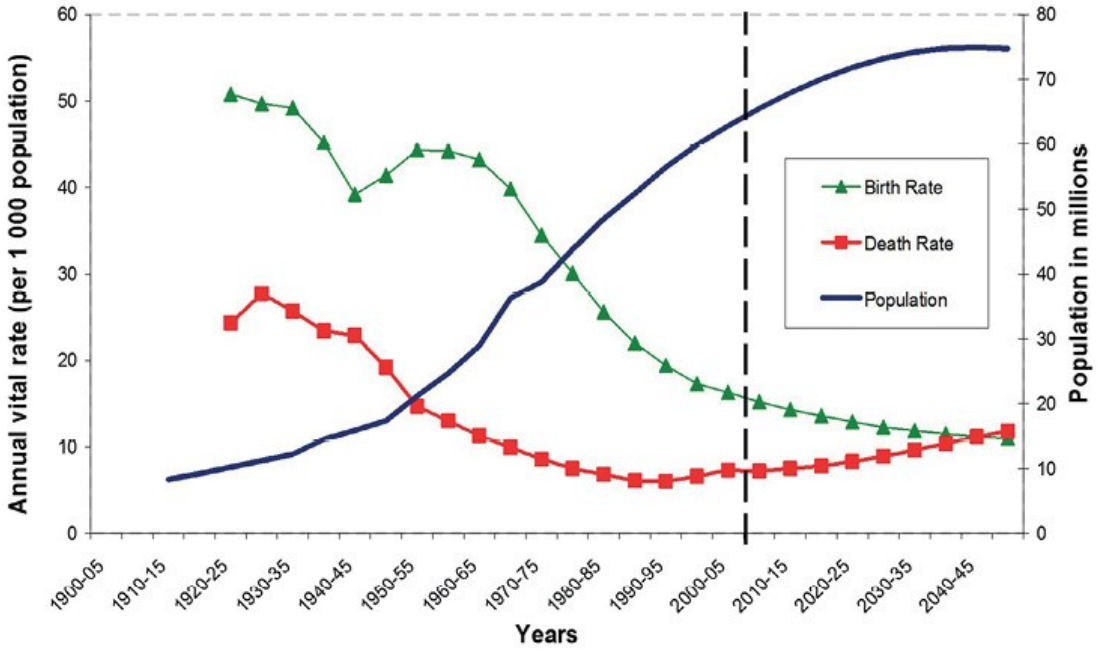


Figure 1-7 The demographic transition in Thailand(Sleigh et al., 2008)

As a result of increased life expectancy and economic growth, exposure to environmental and behavioural risk factors has increased and disease patterns have shifted from infectious towards lifestyle degenerative diseases. This is evidenced by recent changes in the major causes of death and disability among Thai men and women. In 1967, the top causes of mortality among Thai adults were turberculosis and diarrhoea whereas in 2009 the leading cause of death was cancer (Bureau of Policy and Strategy, 2011). In 2004, disability adjusted-life years (DALYs) from non-communicable diseases were already triple those from communicable diseases (Bureau of Policy and Strategy, 2011) and in 2014 non-communicable diseases were estimated to account for over 70% of all deaths in Thailand (World Health Organization, 2014).

1.7.5.3 Health transition

Thailand has experienced substantial social, cultural, and behavioural health-related shifts in recent decades. Examples of these include the introduction of the Universal Coverage Scheme in 2002, which provides free medical care for the entire Thai population, and

various additional schemes that provide health benefits for different types of workers including the Civil Servants Benefit Scheme, the Workman's Compensation Scheme, and the Social Security Scheme (Kelly et al., 2010). Moreover, in recent years, child immunization and family planning services have been introduced equitably across different socioeconomic groups in Thailand (Kongsri et al., 2011). Other major changes relating to Thailand's health transition include women's increasing participation rates in the workforce and the associated reduction in breastfeeding rates (Yimyam and Hanpa, 2014).

1.7.5.4 Nutrition transition

Rapid national economic and socio-demographic changes, including increased urbanization and transnational supermarket infiltration, have led to major dietary shifts in Thailand (Kelly et al., 2014, Yiengprugsawan et al., 2011). The traditional Thai diet consists mostly of rice and fish (Kosulwat, 2002) however a marked shift in dietary intake variety has been observed over the past 40 years leading to an increased intake in animal products, fats and oils, processed sugars, and alcohol (Kosulwat, 2002). For instance, per capita intakes of milk and meat have increased from 7 and 41 grams (g) /per person/per day in 1960 to 66 and 76 (g) /per person/per day in 2003 (Chavasit et al., 2017), respectively. Consumption of sugar nearly tripled from 12.7 kilograms (kg)/person/year in 1983 to 31.2kg/person/year in 2009 (Bureau of Policy and Strategy, 2011) with much of it in the form of sugar-sweetened beverages (Baker and Friel, 2014). Indeed, between 2003 and 2009, the national consumption of carbonated soft drinks doubled from 7.9% to over 16% among Thais aged 15 years or older (Aekplakorn and Satheannoppakao, 2010). Moreover, alcohol consumption has risen from 37.9 L/person/year in 1997 to 45.7L /person/year in 2008 (Bureau of Policy and Strategy, 2011).

The evident dietary shift that has occurred in Thailand over the past few decades is of concern. Unlike the traditional Thai diet (rich in fish, rice, fresh herbs and vegetables) that promotes longevity and prevents disease (Kosulwat, 2002, Montonen et al., 2003) the 'modern' or western diet does not. Also, the new diets have been associated with obesity and T2DM risk (Schulze et al., 2004, Sluijs et al., 2010, Goran et al., 2013). However, longitudinal data are required to determine how emerging diets associate with

emerging T2DM in Thai adults and what aspects of these transitional diets might be beneficial for related health outcomes.

1.7.6 Summary – transitions related to T2DM

Over the past few decades, many LMICs across Southeast Asia have experienced rapid economic development. This has increased urbanization, improved access to labour saving technology, lengthened life expectancy, and altered many health-risk behaviours. The transitions described above provide a logical framework to understand recent increases in T2DM in Asian countries undergoing economic growth. However, longitudinal empirical evidence is required to determine the factors creating a T2DM risk in Southeast Asia, and this includes Thailand.

1.8 Concluding remarks and rationale for this thesis

The global prevalence of T2DM is increasing rapidly, with the majority of the burden expected to occur in LMICs as they experience continued economic development, a demographic shift towards an aging population, and accompanying health risks.

Diagnosing T2DM is complex and is even more challenging when it is assessed in large epidemiological studies where some clinical methods for diagnosis are infeasible. With the prevalence of T2DM projected to keep rising, diabetes identification methods will need to become more feasible logistically and inexpensive enough to deploy when investigating a large number of people. This is particularly true for LMICs where resources are scarce.

There is limited information on the epidemiology of T2DM in LMICs in Southeast Asia. Higher T2DM rates in developing Asian countries indicate that there may be some unique local risk factors operating in these populations. Without identifying local drivers and targeting them in customized preventive policy, health-risks will keep growing with continued economic development and increasing urbanization.

The information presented in this introductory chapter leads to a rationale for investigating T2DM in Southeast Asia. Thailand represents well the issues in play and is influential in the region. As well, Thailand itself is responsible for a steadily growing proportion of the disease burden. Large-scale longitudinal data are required to determine

local causal factors and provide information for prevention of T2DM in the Thai population.

The Thai Cohort Study (TCS), a nation-wide longitudinal epidemiological project, was developed to examine how changing health-risks are affecting health outcomes in Thai adults. The TCS data provide an opportunity carry out some of the studies needed to address the information gap regarding T2DM in LIMCs in Southeast Asia. TCS data can be used to assess the validity of self-report when attempting to detect a large number of cases across the country and to assess the incidence of T2DM and its many risk factors in Thai adults. This information is required to identify the local drivers of T2DM and to guide targeted public health interventions for its control in Thailand.

1.9 Research aim, objectives, and questions

The overall aim of this thesis is to better understand the epidemiology of type II diabetes now emerging in Southeast Asia. To respond to this aim I will use the TCS, a large nationwide 8-year cohort study of the health-risk transition in Thailand.

For T2DM in Thailand, the objectives of this thesis are to:

1) validate self-report of doctor diagnosis for detecting the disease in the population

2) analyse the disease incidence and associated risks

3) assess the direct and obesity-mediated effects of sugar-sweetened beverages

4) investigate the relationship between BMI and T2DM, and calculate population attributable risk

5) determine the association between upstream T2DM risk factors and dietary patterns.

Table 1-2 Research questions, objectives, hypotheses, chapters and relevant studies

Research question	Objective	Hypotheses	Publication title
How valid is self-reported doctor-diagnosed T2DM?	To validate self-report of doctor-diagnosis for detecting the disease in the population	1H1:Self-reports of doctor-diagnosed T2DM are valid in Thai adults 1H2: Self-reports of T2DM can be used to asses trends and determinants in T2DM	Validity of Self-Reported Diabetes in a Cohort of Thai Adults
What is the incidence and what are the risk factors for T2DM?	To analyse the disease incidence and associated risks	2H1: The incidence of T2DM in Thai adults is comparable with other countries undergoing a transition 2H2: Changes that have accompanied the health-risk transition are posing a T2DM risk	Incidence and Risk Factors for Type 2 Diabetes Mellitus in Transitional Thailand: Results from the Thai Cohort Study
How do sugar-sweetened beverages influence T2DM risk?	To assess the direct and obesity-mediated effects of sugar-sweetened beverages	3H1: Frequent SSB intake increases the risk of T2DM in Asian adults 3H2: Obesity mediates a proportion of the SSB-T2DM 3H3: SSB intake increases T2DM risk independent of obesity	Consumption of sugar-sweetened beverages and type 2 diabetes incidence in Thai adults: results from an eight year prospective study
What is the relationship between baseline body mass index and incidence of T2DM in men and women in transitional Thailand	To investigate the relationship between BMI and T2DM, and calculate population attributable risk	4H1: BMI increases T2DM risk at a cut off <25kg/m2 4H2:Over half of T2DM in Thai adults is attributed to excess weight	Body mass index and type 2 diabetes in Thai adults: defining risk thresholds and population impacts
How do socio-economic position and urbanization status associate with dietary patterns in Thai adults?	To determine the association between upstream T2DM risk factors and dietary patterns	5H1: Women are more likely to follow a diet that reduces T2DM risk 5H2:High SEP associates with a healthier dietary pattern in Thai adults 5H3: Urbanization associates with dietary patterns that promote T2DM risk	Social demography of transitional dietary patterns in Thailand: prospective evidence from the Thai Cohort Study

1.10 Thesis structure

The first chapter (Chapter 1) introduces the research topic for this thesis investigating T2DM and the health-risk transition in Thailand. It then presents a synthesis of the current literature, identifies the knowledge gaps in the literature, and outlines the research aim, objectives, questions, and hypotheses.

Chapter 2 provides an overview of the methodological approaches taken in this thesis. It describes the data sources, survey protocols, and statistical techniques used to collect and analyse the data required to address the research questions outlined in this thesis.

Chapter 3 is a published peer-reviewed article that summarizes the literature on self-reported diabetes in epidemiological studies. It then adds to the literature by addressing the first research objective of this thesis. This paper is entitled 'Validity of Self-Reported Diabetes in a Cohort of Thai Adults' and has been published in the Global Journal of Health Science.

Chapter 4 is a published peer-reviewed article that summarizes the literature on T2DM in Southeast Asia and Thailand and its risk factors. It then adds to the literature by addressing the second research objective of this thesis. This paper is entitled 'Incidence and Risk Factors for Type 2 Diabetes Mellitus in Transitional Thailand: Results from the Thai Cohort Study' and has been published in the BMJ Open.

Chapter 5 is a published peer-reviewed article that summarizes the literature on sugar-sweetened beverage intake and T2DM risk in western and Asian populations. It then adds to the literature by addressing the third research objective of this thesis. This paper is entitled 'Consumption of sugar-sweetened beverages and type 2 diabetes incidence in Thai adults: results from an eight year prospective study' and has been published in Nutrition & Diabetes.

Chapter 6 is a published peer-reviewed article that summarizes the literature on the BMI-T2DM relationship in Asian populations. It then adds to the literature by addressing the fourth research objective of this thesis. This paper is entitled 'Body mass index and type 2 diabetes in Thai adults: defining risk thresholds and population impacts' and has been published in BMC Public Health.

Chapter 7 is a published peer-reviewed article that summarizes the literature on transitional dietary patterns and their socio-demographic predictors in Thai adults. It then adds to the literature by addressing the fifth research objective of this thesis. This paper is entitled 'Social demography of transitional dietary patterns in Thailand: prospective evidence from the Thai Cohort Study' has been published in Nutrients.

In chapter 8, I review and connect the five results chapters and provide an overall summary on the T2DM epidemic and its risk factors in Thailand. The strengths and limitations are discussed along with the significance of this work and its implications for public health policy and action. Ideas for further research are also discussed.

2

STUDY METHODS AND PARTICIPANTS

2 Study methods and participants

2.1 Overview

This chapter describes the data sources, survey protocols, and statistical techniques used to collect and analyse the information required to address the research questions outlined in this thesis.

2.1.1 Data sources

The data for this thesis were collected from Thai adults enrolled in the Thai Cohort Study (TCS). From this cohort, three data sources were used for the research reported in Chapters 3-7. The data sources, ethical approvals, protocols, eligibility criteria, and data cleaning methods are summarized below.

2.1.2 Data source 1: The Thai Cohort Study (TCS)

The TCS is a prospective observational study of a large nation-wide cohort of distance learning Open University students. It is a study of health risks and outcomes in transitional Thailand. The overall aims are to investigate how health-risks are changing over time, how they are distributed among Thai adults, and how they affect health status. Also under investigation is the effect of rapid socio-economic development. Appropriate interventions to control and prevent emerging disease epidemics are also considered by the TCS (Sleigh et al., 2008).

To start the TCS in 2005, a 20-page baseline questionnaire was mailed to all 200,000 students enrolled at Sukothai Thammithirat Open University (STOU). A total of 87,151 (44%) students returned their questionnaire and formed the baseline cohort. In 2009, a follow-up questionnaire was sent to all participants of the baseline cohort. Of these a total of 60,569 (70%) were successfully followed-up. In 2013, a further follow-up questionnaire was sent to all participants who responded in 2009; 42,785 (70%) returned a completed questionnaire again in 2013 Table 2.1 shows selected characteristics of the cohort across the three surveys.

Table 2-1 Selected characteristics of TCS participants responding to each survey

Characteristics	Participants in 2005 n (%)	Participants in 2009 n (%)	Participants in 2013 n (%)
Sex	**87,151**	**60,569**	**42,785**
Male	39,484 (45.3)	27,406 (45.3)	19,330 (45.2)
Female	47,659 (54.7)	33,163 (54.8)	23,455 (54.8)
Age			
15-29	46,714 (53.6)	28,681 (47.4)	18,361 (42.9)
30-39	27,320 (31.4)	20,907 (34.5)	15,576 (36.4)
40-49	10,953 (12.6)	9,173 (15.1)	7,399 (17.3)
50 and over	2,145 (2.5)	1,808 (3.0)	1,449 (3.4)
Body Mass Index			
Normal (<23.0)	59,471 (69.2)	40,327 (67.5)	27,937 (66.2)
At risk (23.0-24.9)	12,969 (15.1)	9,484 (15.9)	7,018 (16.6)
Obese (≥25)	13,560 (15.8)	9,953 (16.6)	7,278 (17.2)
Income			
≤10,000	55,434 (65.2)	36,500 (61.6)	24,733 (58.9)
10,001-20,000	20,570 (24.2)	15,729 (26.5)	11,857 (28.3)
≥20,001	8,956 (10.5)	7,042 (11.9)	5,370 (12.8)
Education level			
Junior high school	3,039 (3.5)	2,023 (3.4)	1,325 (3.1)
High school	39,415 (45.4)	25,974 (43.0)	17,594 (41.2)
Diploma/certificate	23,468 (27.0)	16,265 (26.9)	11,384 (26.7)
university	20,985 (24.2)	16,165 (26.8)	12,380 (29.0)
Current residence			
Rural	41,748 (48.3)	29,339 (48.8)	21,201 (49.9)
Urban	44,764 (51.7)	30,819 (51.2)	21,319 (50.1)
Fruit/vegetable Serves per day			
<5 serves	52,486 (62.8)	37,046 (63.5)	26,350 (63.7)
≥5 serves	31,114 (37.2)	21,324 (36.5)	15,026 (36.3)
Smoking			
Never smoked	61,124 (73.6)	42,959 (74.1)	30,646 (74.8)
Ex-smoker	13,409 (16.1)	9,596 (16.6)	6,844 (16.7)
Current smoker	8,539 (10.3)	5,388 (9.3)	3,508 (8.6)
Alcohol intake			
Never drinks	22,712 (26.4)	16,106 (26.9)	11,620 (27.5)
Quit	7,724 (9.0)	5,321 (8.9)	3,633 (8.6)
Occasional drinker	51,371 (59.8)	35,433 (59.2)	24,923 (58.9)
Regular drinker	4,171 (4.8)	2,981 (5.0)	2,116 (5.0)

2.1.2.1 Eligibility for the TCS

STOU students are an informative group of Thai adults that represent the national population well in terms of demography, geography, religion, and socio-economy (Sleigh et al., 2008). All 200,000 distance-learning students enrolled at STOU in 2005 were eligible to take part in the TCS. At baseline, cohort members were adults ranging in age from 15 to 87, of modest means, who were distance-learning students embedded in their communities all over Thailand. Just over half of this cohort was female and living in an urban area of residence. At baseline, cohort members were younger and had a higher level of education than the national Thai population. Accordingly, they were expected to undergo the health-risk transition ahead of their fellow Thais. Thus this cohort can provide information on health and its determinants that will inform trends in the national Thai population in future years.

2.1.2.2 TCS protocols

All TCS participants were asked to self-complete a questionnaire in 2005 and in 2009. Those who were followed-up in 2009 were also asked to complete an additional survey in 2013. In all three surveys, participants were asked questions about their socioeconomic and demographic characteristics (e.g. age, marital status, income, occupation, education level, area of residence), cultural and lifestyle characteristics (e.g. ethnic/religious practices and their dietary intake), health-risk behaviours (e.g. smoking and alcohol intake, transport, seat belt and helmet use), family characteristics (number of children, cause of parental death), and self-reported health outcomes (e.g. dental health, anxiety and depression, weight and health conditions including diabetes). Details on diabetes, the focus of the thesis, are given below.

In 2005, participants were asked '*Have you ever been told by a doctor that you have diabetes (needing or not needing insulin)*'; in 2009 participants were asked '*As a result of a diagnosis by a doctor, have you ever been told that you have diabetes (needing or not needing insulin)*'; and in 2013 participants were asked '*Have you ever received a confirmed diagnosis from a doctor that you definitely have diabetes'*.

The three surveys (2005, 2009, 2013) were developed by TCS investigators including experts from the fields of public health, medicine, anthropology, nutrition, demography, and epidemiology. Where possible, the surveys utilized validated and standardized questions (e.g. the Medical Outcomes (SF8) instrument). Surveys were translated and then back translated to ensure that the meanings of the questions remained stable. All returned surveys were scanned using Scan Devet intelligent character recognition software that creates a linked image and digital data for each questionnaire. Alongside the 2005, 2009 and 2013 surveys, additional validation studies have been conducted to assess the validity and reliability of self-reported data (e.g. for height and weight data).

2.1.2.3 Data processing and variable development

All scanned data were verified by a team of experts at Khon Kaen University who compared the resulting digital data to the scanned data. In addition to this, a group of TCS investigators cleaned and prepared variables for analyses at each wave of follow-up. All actions taken to edit or revise the data and the name and structure of master flies have been described in detail with the project metadata. Categorical and continuous variables were checked for impossible, improbable outlying and missing data points using tabulations and frequency tables, respectively. Data inconsistencies were checked against the original questionnaires for errors and remaining inconsistencies were resolved by discussion among the TCS investigators. Where possible, errors were corrected and where not possible an 'error in data' code was given.

For the purpose of this thesis, additional variables have been prepared. Variables for the main outcome of interest in this study were derived as follows: for diabetes in 2005 and 2009 'yes' responses to having diabetes (needing insulin or not) were combined and considered as diabetes; those responding 'no' on both 2005 and 2009 surveys were considered as not having diabetes. In 2013, there was no specific question on insulin. A response of 'yes' meant having diabetes and 'no' meant not having diabetes. If the participants said 'I am at risk' this was considered as not yet having diabetes. Other decisions regarding how variables were used for the different research questions in this research are outlined specifically in each chapter.

2.1.2.4 Ethics

The chief TCS investigators obtained ethical approval for TCS data from Sukhothai Thammathirat Open University Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocols 2004/344, 2009/570). All participants gave informed written consent. TCS participants were advised that they were free to withdraw from the research at any time.

2.1.2.5 Use of TCS data in the thesis

In this thesis, the first research component to use TCS data was the validation study. This involved generation of additional data as described for data source two (section below) and in Chapter 3.

Other components of the thesis to use TCS data were the incidence study, the SSB study, and the BMI study (Chapters 4, 5 and 6). Study participants for these three components included TCS members who were followed from 2005 to 2013 and did not have a missing response to the TCS diabetes survey question in 2013. Participants who reported diabetes at baseline (N=902) and those who reported having diabetes in 2009 and not in 2013 (N=180), mostly women with gestational diabetes, were excluded from analyses reported in Chapters 4, 5 and 6. Details are given in each chapter regarding criteria for inclusion.

2.1.3 Data source 2: diabetes validation study for TCS participants

In 2015, as part of the research for this thesis, the validity of self-reported diabetes status was confirmed using physician telephone interviews. All eligible TCS participants (see next section below) were mailed an information sheet describing this validation study before being contacted by phone for the physician interviews (Appendix A).

2.1.3.1 Eligibility for validation study

TCS members were eligible to participate in the validation study (Chapter 3) if:

- they were followed up in 2013 (i.e. had eight years of observation), and
- in 2005 they responded ‘no’ to the TCS survey question ‘Have you ever been told by a doctor that you have diabetes (needing or not needing insulin)’, and

- in 2009 they had responded to the TCS survey question '*As a result of a diagnosis by a doctor, have you ever been told that you have diabetes (needing or not needing insulin)*' and/or;

- in 2013 they responded to the TCS survey question '*Have you ever received a confirmed diagnosis from a doctor that you definitely have diabetes'* .

From a list of potentially eligible participants, we attempted to contact all incident cases (first reported a diagnosis of diabetes in either 2009 or 2013) (n=878) as well as a random sample (2%) of participants who never reported a diagnosis of diabetes (n=650) (Figure 2-1).

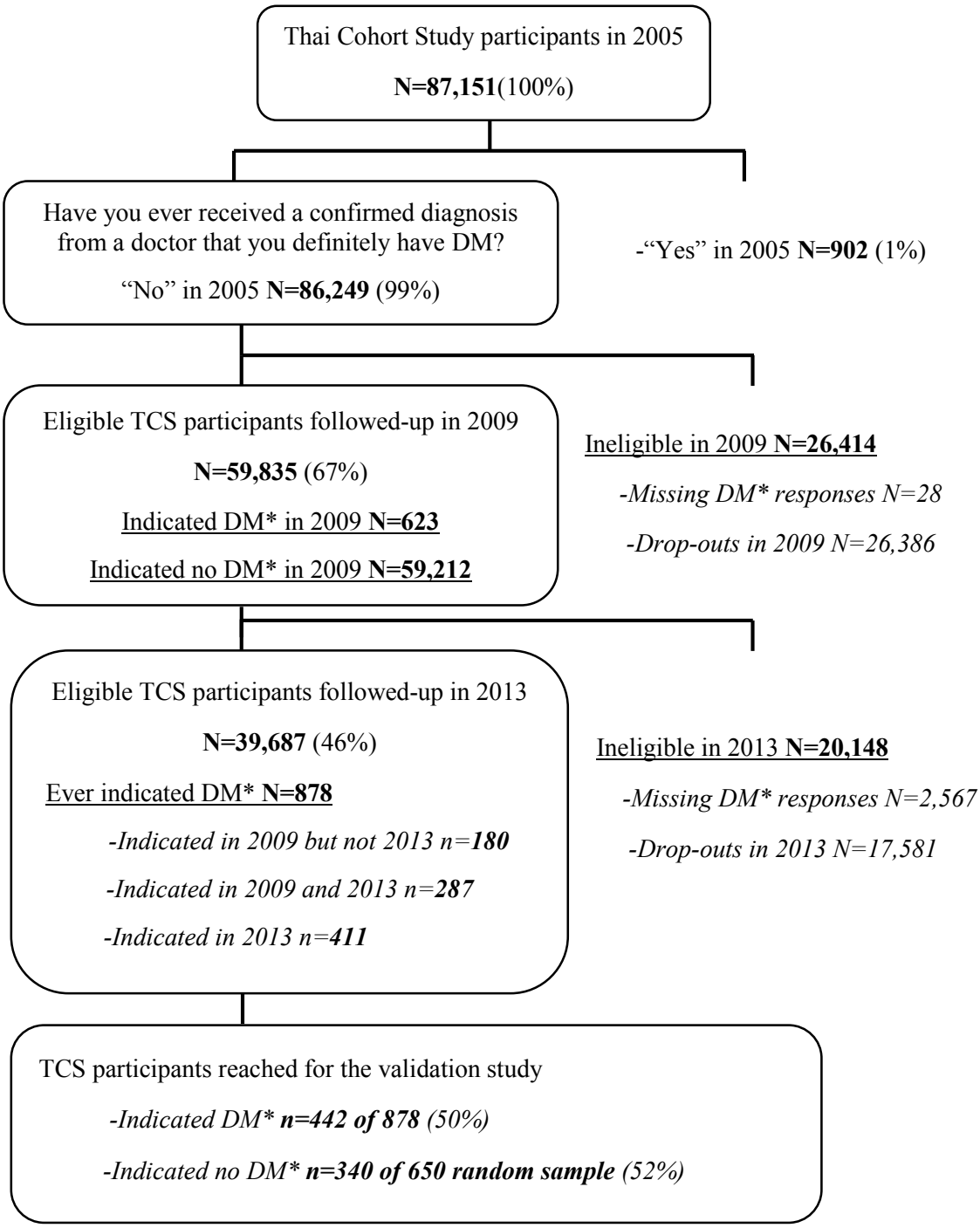


Figure 2-1 Flow chart for the validation study of self-reported diabetes

*DM diabetes mellitus

2.1.3.2 Protocols

The Thai physician used an interview protocol to determine diabetes status. I developed this protocol in consultation with a group of five physicians (four Australian and one Thai) and one additional public health nutritionist, following the American Diabetes Association's (ADA) classification guidelines for diagnosing diabetes (Appendix A). The protocol was translated and back translated to ensure accuracy. Using this protocol, the Thai physician was able to confirm whether participants had been diagnosed with diabetes and record information from participants regarding how they were diagnosed with diabetes; and whether or not they had been diagnosed with transient or type 2 diabetes. I entered all interview data into a statistical software package.

2.1.3.3 Data processing and variable development

All physician interview data were cleaned and categorized in consultation with the interviewing physician. Three variables were then created: 1) the first classified the sampled participants according to whether or not they were successfully contacted for interview; 2) the second classified the responding participants as having correctly reported a diagnosis of diabetes; and 3) the third to classified participants according to whether or not they had T2DM, transient diabetes, or no diabetes based on the physician interviews.

2.1.3.4 Ethics

I obtained ethics approval for the diabetes validation study from the Australian National University Human Research Ethics Committee (protocol 2014/782). All participants gave their informed oral consent prior to beginning the interviews. TCS participants were advised that they were free to withdraw from the research at any time.

2.1.4 Data source 3: dietary study for TCS participants

To collect data for the dietary study, in 2015 all eligible TCS participants were mailed an information sheet describing the study along with the dietary survey (Appendix B).

2.1.4.1 Eligibility

Participants who completed all three TCS questionnaires (2005, 2009, and 2013) were eligible for the dietary study (N=42,785). We invited a random sample of 2,400 TCS

members to complete the additional dietary survey in 2015. A total of 1090 (45%) completed and returned their dietary surveys. Of these, 15 (men n=10, women n=5) did not respond to >10% of their FFQ questions and were excluded. Analyses were based on 1075 participants.

2.1.4.2 Data collection tools

All dietary data in 2015 were collected using a dietary survey. I developed this survey in consultation with my supervisory team. The dietary survey incorporated the Thai National Health Examination Survey food frequency questionnaire (FFQ) (Appendix B). The Thai FFQ has been previously validated in the national Thai population and has been used to determine dietary patterns and their association with health outcomes. I obtained permission from a representative from the Thai Ministry of Public Health to use this FFQ in my research. The FFQ was already written in Thai but the remainder of the survey was translated into Thai and back translated to English to ensure accuracy. All returned surveys were scanned using a Scan Devet intelligent character recognition software that creates a linked image and digital data for each questionnaire.

2.1.4.3 Data processing and variable development

All scanned data were verified by a team of experts at Khon Kaen University who compared the resulting digital data to the scanned data. In addition to this, I cleaned the data in consultation with a nutritional epidemiologist and with guidance from the literature (Willett, 2012, Thorpe et al., 2016). Accordingly, participants were excluded from this study if responses to >10% of food consumption items were missing while all other missing FFQ items were considered not consumed. FFQ responses for each item were converted into daily intake equivalents as follows: ‘don’t eat at all’=0, ‘less than once per month’ (0.5/30=0.02), ‘1-3 times per month’(2/30=0.07), ‘1-3 times per week’ (2/7=0.28), ‘4-6 times per week’(5/7=0.71), ‘once per day’=1, or ‘more than once per day’=2.5. All 44 food items were allocated into 30 mutual foods groups (Supplement 7.1).

2.1.4.4 Ethics

I obtained ethics approval for the dietary study from the Australian National University Human Research Ethics Committee (protocol 2015/068). All study participants sent back their written consent along with their completed surveys. TCS participants were advised that they were free to withdraw from the research at any time.

2.1.4.5 Use of dietary survey data in this thesis

The dietary data collected in 2015 were used to support the analyses in Chapter 7.

2.2 Conceptual framework

2.2.1 The 'Health-Risk' transition study

Thai Cohort Study investigators adopted a multilevel eco-social model to determine the population health status in Thailand and its complex drivers (Figure 2-2). This model considers the multi-level health-risks that play a role in Thailand's health-risk transition.

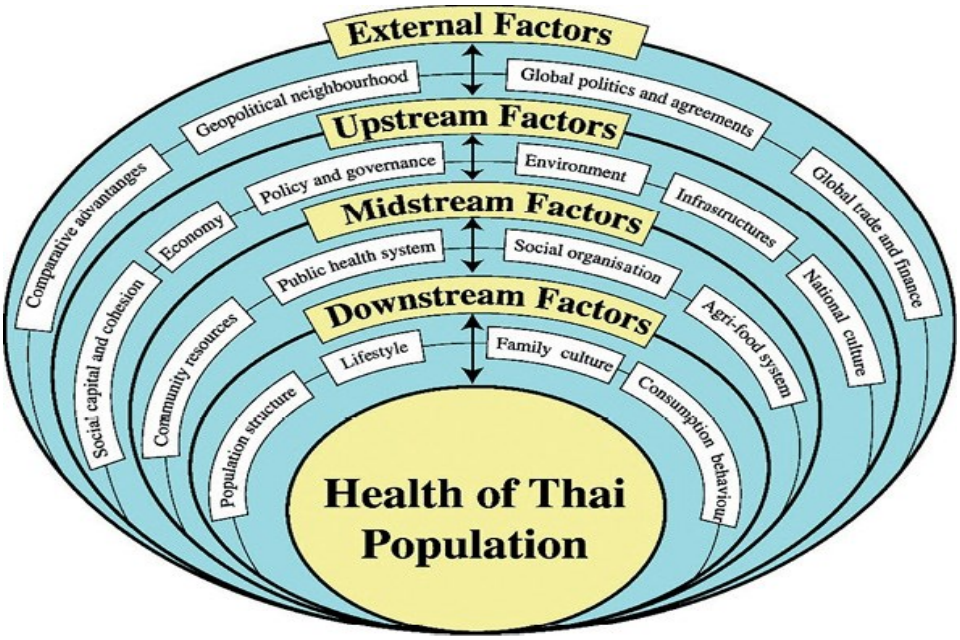


Figure 2-2 Multilevel eco-social health model (Sleigh et al., 2008)

2.2.2 Risk factors of T2DM in transitional Thailand

For the purpose of this thesis, the TCS eco-social model has been further adapted to show clearly the multi-level drivers of type 2 diabetes mellitus. Hence, the following framework has been used to guide the overall research design of this study (Figure 2-3). This research investigated T2DM and its multi-level risk factors in TCS participants.

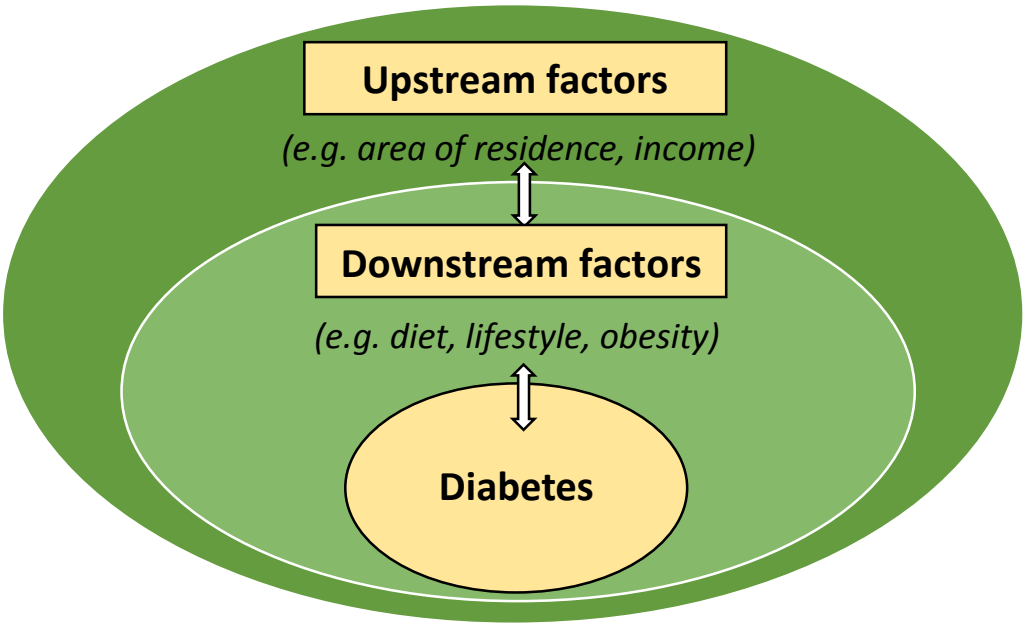


Figure 2-3 Conceptual framework for risk factors of T2DM in transitional Thailand

2.3 Statistical analysis

The statistical methods for this work are described in detail in each of the methods sections of Chapters 3 to 7 and are summarized here. In Chapters 3 to 6, I compared the distribution of exposures of interest and potential confounders in participants with and without incident diabetes. I then used logistic regression to calculate crude and covariate-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) to assess longitudinal associations between exposures of interest and T2DM. Non-linear associations were modelled using restricted cubic splines. In Chapter 7, I used principle component analysis to identify dietary patterns. I then used linear regression to estimate standardized coefficients (ßeta) and 95% CIs to assess associations between socio-demographic measures and dietary intake pattern scores. Possible variable interactions were also assessed throughout using stratification and by adding interaction terms and testing their statistical significance.

Development of the final models used to explore the associations between the exposures of interest with diabetes or dietary patterns consisted of a multifaceted approach. Initially, I constructed a theoretical causal model based on the literature using directed acyclic graphs (Appendix C). Directed acyclic graphs (or DAGs) are diagrams that help describe causal relationships between variables. These are drawn in accordance with causal rules and assumptions (e.g. causes (X) must precede effects (Y) and therefore the graph cannot be cyclic). Based on these rules, which are mathematically grounded, it is possible to translate these causal diagrams into statistical models. In this way, DAGs can assist with selecting covariates for regression analyses, identifying potential bias and error, and understanding analyses of direct and indirect effects (Greenland et al., 1999) (Rothman et al., 2008).

After considering the theoretical causal model, I used a 'change-in-estimate' approach to identify confounders. This is a method for selecting variables based on changes in the estimated exposure effect (e.g. >10%) (Rothman et al., 2008). As well, I used likelihood ratio tests to assess whether interaction terms were statistically significant ($p<0.05$).

2.4 Summary

This chapter outlined the methods used to collect, prepare and analyse the data for the various studies of this thesis. In each of the following five chapters, I present additional details in journal article format regarding the specific statistical methods used to answer each study question and the findings for each research question. The published articles in each chapter have been prepared in accordance with the requirements of each specific journal.

3

VALIDITY OF SELF-REPORTED DOCTOR-DIAGNOSED TYPE 2 DIABETES IN THAI ADULTS

3 Validity of self-reported doctor-diagnosed T2DM in Thai adults

Chapter 3 is a peer-reviewed article that has been published in the *Global Journal of Health Science*. It addresses Objective 1: to validate self-report for detecting the disease (T2DM) in the population. Physician telephone interviews to validate questionnaire responses were conducted in 2015 with a sample of participants who self-reported T2DM (N=442) and with a sample of participants who self-reported no T2DM (N=340). Results demonstrated the high validity of questionnaire self-reported doctor diagnosed T2DM and support the accuracy of the subsequent analyses carried out in Chapters 4-6.

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Validity of Self-Reported Diabetes in a Cohort of Thai Adults

Keren Papier[1,2], Susan Jordan[2], Chris Bain[1,2], Catherine D'Este [1], Prasutr Thawornchaisit[3], Sam-ang Seubsman[4] & Adrian Sleigh[1]

[1] National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, Australia

[2] Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane, Australia

[3] Lerdsin General Hospital, Bangkok, Thailand

[4] Thai Health-Risk Transition Study, School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi, Thailand

Correspondence: Keren Papier, QIMR Berghofer Medical Research Institute, 300 Herston Rd, Brisbane, 4006 QLD, Australia. Tel: 61-7-3845-3571. E-mail: Keren.Papier@anu.edu.au

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Abstract

Background: Much of South East Asia is experiencing an epidemiological transition. In Thailand, chronic disease has emerged and the prevalence of diabetes has tripled. As part of a large cohort study of the Thai transition to chronic disease, we gathered data on self-reported diabetes. Epidemiological studies commonly ascertain such data by self-report but the validity of this method has not been assessed in Thailand. Therefore, we aimed to investigate the validity of self-reported type 2 diabetes (T2DM) in Thai adults participating in the Thai Cohort Study (TCS).

Methods: Data were collected by mailed questionnaire from adults involved in the TCS, a nationwide community-based longitudinal health study of distance learning adult students enrolled at Sukhothai Thammathirat Open University. Participants were surveyed in 2005, 2009 and 2013. We sampled all participants with self-reported T2DM status (878 cases) for telephone interview with our study physician along with a random selection of 650 participants who self-reported not having diabetes in all three TCS surveys. These physician telephone interviews allowed us to validate self-reported questionnaire responses.

Results: Questionnaire self-report of diabetes slightly over-estimated the incidence of T2DM in this cohort; the overall proportion of confirmed T2DM cases was 78%. Participants with a consistent pattern of diabetes reporting at the 2009 and 2013 questionnaire follow-ups had the highest validity of self-reported responses (96%; 95%CI 92.9-99.1).The lowest proportion of confirmed T2DM cases was recorded among participants who reported diabetes in 2009 and not in 2013 (32%)(95%CI 22.6-41.4), mostly young women with transient (gestational) diabetes.

Conclusions: Our results, derived mainly from young, educated Thai adults nationwide, show that self-reported doctor diagnosed T2DM is a feasible and acceptable method for assessing diabetes in epidemiological studies.

Keywords: cohort study, diabetes mellitus, type 2, self-reported diabetes, Thailand, validation study

1. Introduction

Many developing countries have undergone rapid economic growth over the past 50 years and this has transformed diets, behaviors and disease. There have been great health benefits associated with this transition, including decreased childhood mortality and reduced prevalence of infectious diseases. But there has also been a widespread adoption of unhealthy behaviors (such as smoking and lack of exercise), along with a concomitant emergence of unhealthy environments (such as urban slums and air pollution), and a transformation of food systems and agrarian diets into modern supermarkets and industrialized food. These changes lead to the emergence of chronic and degenerative diseases. Collectively, these shifts in behavior, environment, diet, and disease have been labelled the 'health-risk transition' (A. Sleigh & Seubsman, 2015). As part of the transition, T2DM has emerged as a major cause of morbidity in many middle-income countries, including Thailand (Ramachandran, Wan Ma, & Snehalatha,

2010). With over 4.0 million Thai adults estimated to have diabetes, Thailand is now one of the most affected countries in Asia (Chan et al., 2009; International Diabetes Federation, 2015).

To respond to the emerging non-communicable disease epidemic in Thailand, and understand the local risk factor dynamics, researchers from Thailand and Australia have established the 'Thai Cohort Study', a nation-wide investigation of the ongoing 'health-risk transition' (A. C. Sleigh, Seubsman, Bain, & The Thai Cohort Study Team, 2008). Like many large-scale epidemiological studies, the TCS used self-completed questionnaires to collect information on risk factors and disease, including diabetes. Collecting health information via self-report is a feasible and convenient method for obtaining population data but questions arise over accuracy of this method. Responses by study participants may vary depending on their personal characteristics, including education level and perceptions and understanding of disease (Goto et al., 2013; Okura, Urban, Mahoney, Jacobsen, & Rodeheffer, 2004).

Several studies have suggested that a diagnosis of diabetes is accurately reported by study participants however this work was carried out in cohorts restricted to women (Manson et al., 1991; Pradhan, Manson, Rifai, Buring, & Ridker, 2001; Rylander, Sandanger, Engeset, & Lund, 2014) or people within a specific age range (Comino et al., 2013; Goldman, Lin, Weinstein, & Lin, 2003; Margolis et al., 2008). Among studies conducted within larger or more heterogeneous cohorts, the accuracy of self-reported diabetes varied by socio-demographic characteristics (Okura et al., 2004; Yuan, Liu, Wu, Zou, & Li, 2015) or by ethnicity (El Fakiri, Bruijnzeels, & Hoes, 2007; Goto et al., 2013). Socio-demographic characteristics such as older age (with cognitive decline) (Sherbourne & Meredith, 1992) and lower education level (with reduced health literacy) (Yuan et al., 2015) may associate with reduced accuracy of self-reported diabetes. Little research has assessed the accuracy of self-reported health information among Asian populations, although it has been suggested that there may be higher levels of misreporting than in western populations (Goldman et al., 2003; Goto et al., 2013; Yuan et al., 2015).

Accuracy of self-reported health status among Asian populations may link to traditional cultural beliefs. In some Asian countries (including China and Thailand), traditional medicine may be practiced alongside and/or as part of the healthcare system (Chokevivat, Chuthaputti, & Khumtrakul, 2005; Hesketh & Zhu, 1997). Treatment for health conditions may be sought using traditional and/or modern medicine approaches (Yuan et al., 2015). As a result, traditional medical perspectives and/or treatment may lead to misreporting or under-reporting in Asian populations. For example, individuals using traditional Chinese medicine may under-report hypertension (Goldman et al., 2003) since high blood pressure may not be considered as a disease according to traditional Chinese medicine (Goldman et al., 2003). In contrast, Chinese adults self-report diabetes more accurately when also questioned about use of traditional Chinese anti-diabetic medicine (Yuan et al., 2015). Whether similar issues are relevant in Southeast Asian populations is not known. Specifically, the validity of diabetes self-report has not been investigated in the Thai population. Many Thais practice traditional Thai medicine which is highly influenced by both Theravada Buddhism (the main school of Buddhism practiced in Thailand) and by traditional Chinese medicine (Offringa, 2014). Accordingly, field studies of self-reported diabetes among Thais may be affected by traditional cultural beliefs just as noted in Chinese populations and this might influence the epidemiological information.

Therefore, we validated questionnaire self-report of doctor-diagnosed T2DM in Thai adults participating in the TCS by comparing physician interview data to the questionnaire data. We also investigated whether the validity of self-reported questionnaire T2DM was associated with personal socio-demographic characteristics. We then determined the impact that any potential reporting bias may have on cumulative incidence estimates for T2DM.

2. Methods

2.1 Source Population

In 2005 all 200,000 enrolled Suhkkothai Thammathirat Open University (STOU) students were mailed a detailed baseline questionnaire that covered a wide range of topics including socio-demographic characteristics, lifestyle behaviors and self-reported health outcomes. These students were adult distance learning students of modest means aspiring to use education for self-improvement. As such they are expected to undergo the 'health-risk transition' dynamics ahead of their fellow Thais. Of the total 87,151 (100%) students who returned their questionnaire in 2005, 60,569 (69%) were successfully followed up in 2009 and 42,785 (49%) were followed up again in 2013.

2.1.2 Ascertainment of Diabetes Status

In all three surveys (baseline, four-year follow-up, and eight-year follow-up), cohort members were asked whether they had ever been told by a doctor that they had diabetes. The questionnaire did not ask participants to specify the

type of diabetes (Type 1, Type 2, gestational, etc). Therefore all those who ticked 'yes' to this question have been classified as self-reported cases of diabetes mellitus (with the type of diabetes not specified). This included a small group who reported 'yes' in 2009 but reverted to 'no' at follow-up in 2013.

2.1.3 Participant Selection for the Validation Study

Figure 1 shows how participants were selected for this validation study. We excluded the 902 participants in the original TCS cohort who reported doctor-diagnosed diabetes at baseline (2005). Exclusion of baseline prevalent cases ensured our focus was on current diagnostic practices, as incident cases (reported in 2009 and 2013) were of recent onset and would capture outcomes of the 'health-risk transition'. Of those not excluded, participants who completed both follow-up questionnaires (2009, 2013) were sampled for the current study. This allowed us to assess whether an individual's sequential reporting pattern over the 2009 and 2013 follow-up surveys influenced their likelihood of a valid self-reported diagnosis. Those who reported doctor-diagnosed diabetes for the first time in either of the follow-up questionnaires were considered as self-reported incident cases for our study and all 878 were included in the validation sample. Those who reported not having diabetes in all three of the TCS surveys (2005, 2009, 2013) were considered non-cases (n=38,809), of whom we randomly sampled 650.

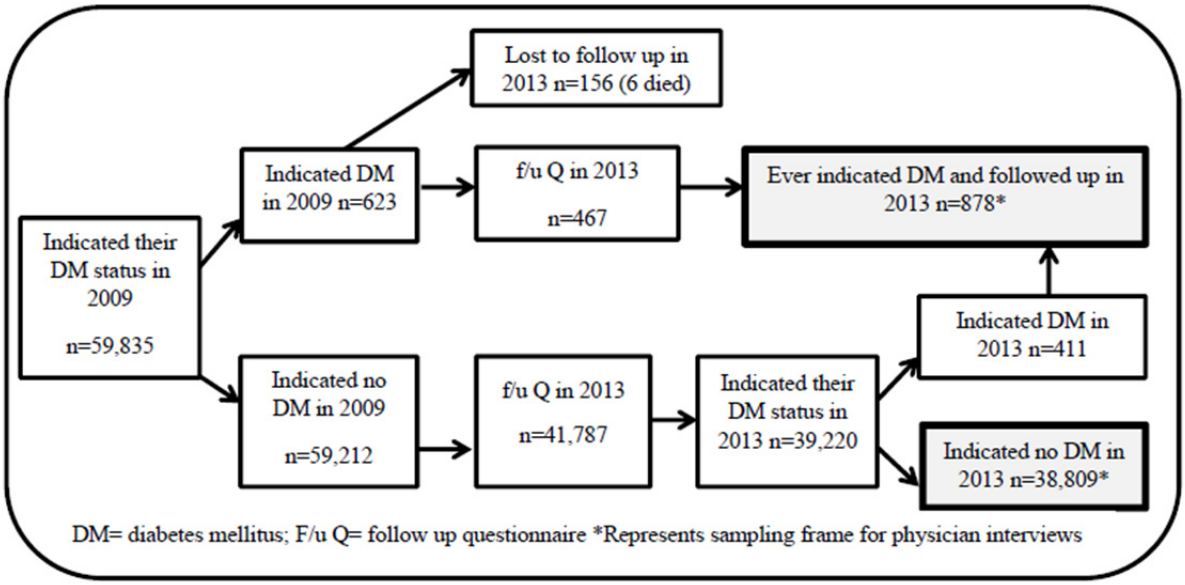

Figure 1. Ascertainment of diabetes cases in Thai Cohort Study participants

Participants* selected based on self-reported diabetes status in 2005, 2009 and 2013.

*The self-reported positives in 2005 were excluded (n=902) as were those missing in 2009. The 59,835 remaining persons were subjected to the sequential process involved in the validation and the numbers of persons in each category as shown in the figure above.

2.2 Data Collection

We used telephone interviews undertaken by a practicing Thai physician to confirm the validity of self-reported doctor-diagnosed T2DM and transient diabetes. Medical record review and/or blood sampling for this nationally dispersed cohort was not logistically feasible. Furthermore, blood measures alone can be uninformative or even misleading for those with diabetes who are receiving treatment and whose blood glucose levels have normalized.

The same Thai physician conducted all interviews to exclude the potential for variation between interviewers. He was selected because of his previous experience with eliciting medical information from the TCS cohort, his knowledge of the use of traditional Thai diabetes medication, and his sensitivity to the culturally specific language required to attain information about such usage.

2.2.1 Interview Procedure for Validation Study

Potential participants were first sent an information sheet describing the validation study and inviting their participation before they were telephoned. The information emphasized that participation was not compulsory and it would be entirely their choice to take part or not. Then, up to three attempts were made to telephone each person

over a 6 week period between May and June 2015. The physician received verbal consent from each interviewee before conducting the interview. After receiving consent, the physician interviewed the sampled participants and progressively characterized each person according to the algorithm in Figure 2.

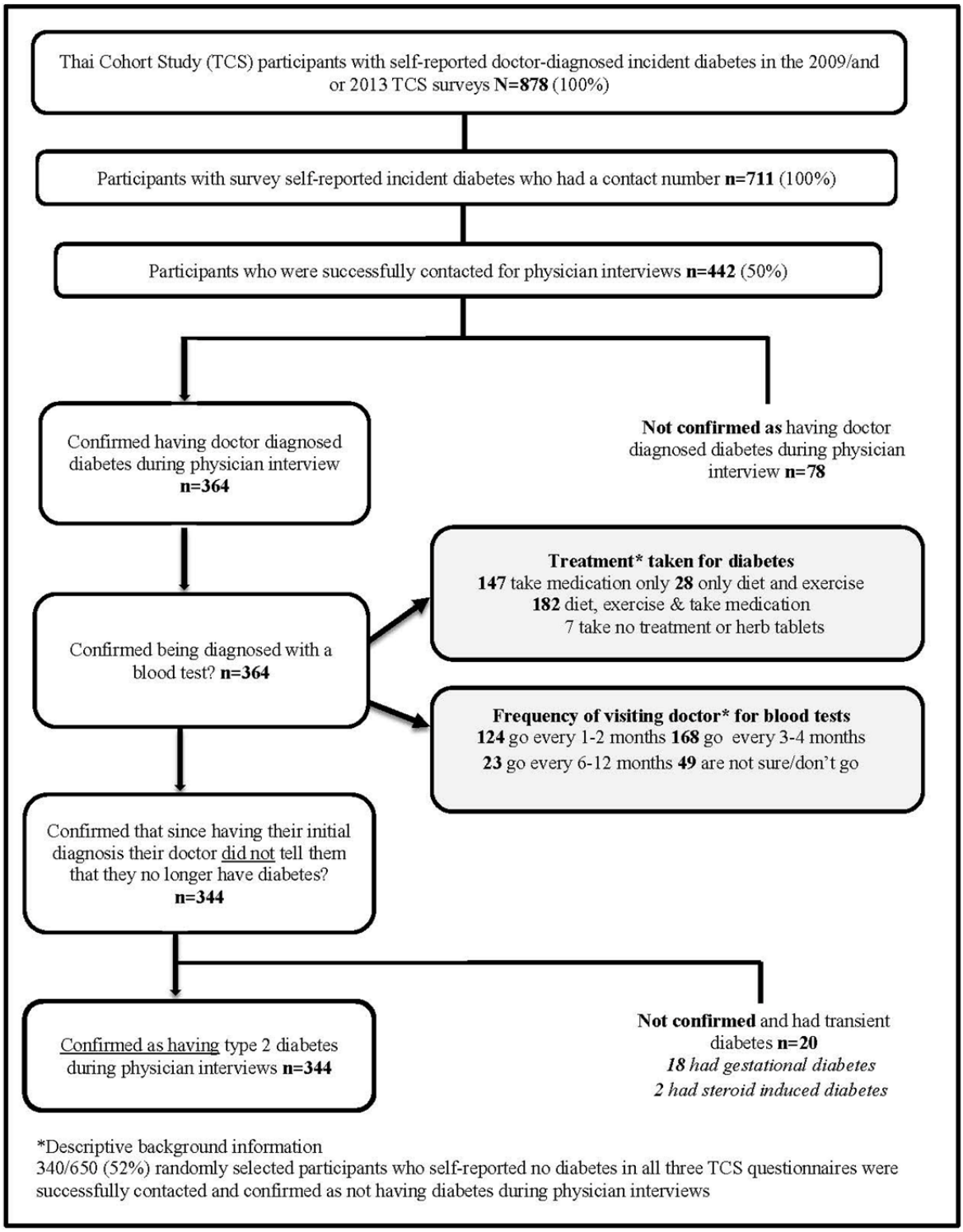

Figure 2. Algorithm used to determine type 2 diabetes status during physician interviews

Physician interviews* were used to determine type 2 diabetes status among sampled participants.

Cases and non-cases were determined using an interview protocol and using the above algorithm.

2.2.2 Ascertainment of Diabetes Cases Based on Physician Interviews

Type 2 diabetes status was determined by an algorithm incorporating the participants' answers to a standard physician interview protocol. The protocol was developed by a group of five physicians (four Australian and one Thai) and two public health nutritionists, following the American Diabetes Association's (ADA) classification guidelines for diagnosing diabetes (American Diabetes Association, 2010). The ADA guidelines are the most commonly used criteria for diagnosing diabetes globally (Shaw, Sicree, & Zimmet, 2010) and are used by researchers and health professionals in Thailand (Aekplakorn et al., 2011). Accordingly, the protocol included questions probing about blood glucose testing and if it had occurred and blood glucose cut off criteria used in the participants' diagnoses of diabetes, as well as the treatment and names of medications prescribed to participants by their physician. The interviewer asked about the frequency of physician check-ups and the types of tests taken during medical visits. Finally, those reporting diabetes were questioned further about transient disease triggered by pregnancy, surgery, use of steroids or other factors. The algorithm used for ascertaining T2DM status based on participants' answers is shown in Figure 2.

2.3 Statistical Analysis

Participants who self-reported diabetes were classified firstly as having correctly reported a diagnosis of diabetes mellitus. They were then classified according to whether or not they had T2DM or transient diabetes based on interviews by our study physician as outlined in Figure 2. It was noted if the transient diabetes was due to pregnancy, surgery, medication, or illness. The sample of participants who self-reported no diabetes in all three surveys were also interviewed by the study physician to confirm their status.

2.3.1 Validation of Self-Reported Questionnaire Data

Amongst the contacted participants, we calculated the proportion of valid self-reported questionnaire responses by dividing the number of physician interview-confirmed T2DM cases by the total number of participants who self-reported diabetes in 2009 and/or 2013. We also confirmed the proportion of validated non-cases by dividing the number of physician interview-confirmed non-cases by the total number of participants who self-reported not having diabetes in all three of the TCS surveys. We then assessed whether the proportion of physician-interview confirmed T2DM cases varied according to various socio-demographic characteristics previously found to be associated with the accuracy of self-reporting diabetes (Molenaar, Van Ameijden, Grobbee, & Numans, 2007; Okura et al., 2004).

We wanted to assess which factors were associated with the correct self-reporting of T2DM separately for self-reported cases and self-reported non-cases. To do this we undertook logistic regression analysis including only the self-reported cases to investigate the socio-demographic characteristics associated with self-reported questionnaire and physician telephone interview agreement (with a binary outcome of no/yes for agreement). A likelihood ratio test was used to assess the significance of the variables in the model. A two sided significance level of 0.05 was used. The regression model included all physician interview confirmed T2DM cases. We then repeated these analyses including all of the physician-interview-confirmed diabetes cases (both T2DM and the transient diabetes cases).

We then investigated how the sequential reporting pattern over the 2009 and 2013 follow-up surveys influenced the likelihood of a valid self-reported diagnosis of T2DM in 2013. Accordingly, we calculated the proportion of validated cases amongst 1) those who self-reported incident diabetes in both 2009 and 2013; 2) those who reported diabetes for the first time in 2013; and 3) those who reported diabetes in 2009 and subsequently reported no diabetes in 2013.

2.3.2 Incidence of T2DM Accounting for the Effect of Misclassification

We also determined the impact that reporting error may have had on estimates of cumulative incidence of T2DM in the cohort. A corrected cumulative incidence was calculated in two ways. We used the proportion of reporting error detected in 2009 incident cases amongst the contacted group to calculate a corrected cumulative incidence among the entire group of 2009 self-reported cases including those who did not participate in the interviews. The same procedure was carried out for the entire group of 2013 self-reported cases using the proportion of error detected in the 2013 self-reported cases who were contacted.

We also carried out a sensitivity analysis to allow for the possibility that the amount of reporting error might be different among the group of participants who were lost-to-follow-up and thus did not participate in the telephone interviews. In this analysis we considered the effects of false positive probabilities by calculating a corrected cumulative incidence for the entire group of 2009 self-reported cases using false positive probabilities ranging between 10% and 50% for participants who did not participate in the interviews and were lost-to-follow up. All

analyses were carried out using Stata (version 13.0).

2.3.3 Sample Size, Power, Precision

Sample size consideration for this study was guided by findings from previous validation studies conducted with Asian cohorts (Goto et al., 2013; Yuan et al., 2015). We expected that half of the selected cohort members who the physician attempted to contact would be reached by phone and would agree to take part in the interview (Kelly, Seubsman, Banwell, Dixon, & Sleigh, 2014). Accordingly, of the total 878 self-reported diabetes cases we expected to successfully follow-up approximately 440. A sample of 440 participants with diabetes would allow estimation of an expected correct reporting proportion of 80% (Goto et al., 2013; Yuan et al., 2015) with 95% confidence interval within +/- 4%. With a higher proportion of correct reporting expected among non-cases (85%), a smaller sample of 325 participants without diabetes would allow for the estimation of 95% confidence interval within the same precision of +/- 4%.

Of the 442 self-reported cases, we expected that 80% (354 participants) would be verified as having T2DM and that 20% (88 participants) would not be verified as having T2DM. Thus, using an expected reporting error of 20%, 80% power and 5% significance level, we would be able to detect a 15% difference in socio-demographic characteristics between those who were and were not confirmed as correctly self-reporting T2DM and between participants who were and were not confirmed as having correctly self-reported diabetes (both T2DM and the transient diabetes cases) during physician interviews.

3. Results

Table 1 displays the baseline characteristics of the self-reported cases and non-cases that were selected for the physician telephone interviews. Among the self-reported cases, 711 of 878 had contact phone numbers and among the 650 non-cases 616 had contact phone numbers and were invited to participate. Of the participants who were selected for interviews, 442 (50%) self-reported cases and 340 (52%) self-reported non-cases were successfully contacted for interview. All participants with whom the physician made contact participated in the study. Among the contacted cases, the median age at baseline was 39.5 (minimum 19, maximum 64) and 52% were male. Among the contacted non-cases just over half were female (54%), and their median age at baseline was 31.5 (range 18 to 78).

Overall the socio-demographic characteristics of those interviewed and those who could not be contacted were similar for self-reported cases and for non-cases (all p-values >0.05). Differences were observed between cases who were interviewed and cases who were not interviewed for monthly income level (p=0.02) (higher income in those interviewed) and between non-cases who were interviewed and non-cases who were not interviewed for age (p=0.02) (lower age in those interviewed).

The physician interviews confirmed that 344 of the 442 (78% (95%Confidence Interval (CI)) 74-82%) contacted cases reporting a new diagnosis of diabetes in either the 2009 or 2013 surveys had incident T2DM (shown in figure 2). Of the 98 cases that were not confirmed as having T2DM, twenty percent were found to have had transient diabetes mellitus (18 gestational and two steroid-induced diabetes). The majority of these transient cases self-reported diabetes in 2009 but not in 2013. Of the remaining 78 non-confirmed cases, the majority indicated they self-reported diabetes because they were told by their physician that they had high blood glucose and were at risk of developing diabetes. The other participants indicated that they had misunderstood the questionnaire and thought that it was asking if they had ever been tested for diabetes. All 340 (100%) participants who indicated in both 2009 and 2013 that they had not been diagnosed with diabetes were found to have reported their disease status correctly.

The proportions of self-reported diabetes cases validated by physician interviews according to various socio-demographic characteristics are shown in Table 2. The overall proportion of all confirmed self-reported diabetes cases (including participants with T2DM and with transient diabetes) was high (82%) and was similar across all socio-demographic characteristics. The overall proportion of confirmed self-reported T2DM diabetes cases was high (78%). Slight differences in the proportion of confirmed cases of T2DM were seen between males and females (82% versus 71% p<0.01) and between participants aged over 40 and those aged under 40 (84% versus 72% p<0.01).

Table 1. Baseline characteristics for participants and non-participants selected for physician interviews to validate self-reported diabetes status

Baseline characteristics	**Ever reported incident diabetes**			**Never reported incident diabetes**		
	Participants N=442* n(%)	Non-participants N=436* n(%)	$P^{\dagger}$	Participants N=340* n(%)	Non-Participants N=310* n(%)	$P^{\ddagger}$
Sex			0.29			0.48
Male	282(52)	263(48)		143(51)	139 (49)	
Female	160(48)	173(52)		197(54)	171 (46)	
Age			0.14			0.02
15-29	58(41)	82 (59)		147(47)	163 (53)	
30-39	168(53)	149 (47)		118(54)	101(46)	
40-49	158(51)	150(49)		69(64)	38 (36)	
50 and over	58(51)	55(49)		6(43)	8(57)	
BMI-Asian cut offs			0.41			0.27
Underweight ($\leq$18.49)	5(38)	8(62)		48(54)	40 (46)	
Normal (18.5-22.9)	84(47)	95(53)		176(51)	171(49)	
At risk (23.0-24.9)	79(51)	76(49)		58(53)	52(47)	
Obese I (25.00-29.9)	189(53)	166 (47)		45(51)	43(49)	
Obese II ($\geq$30.0)	74(46)	87(54)		10(83)	2(17)	
Income			0.02			0.10
$\leq$10,000	147(44.0)	187 (56)		197(49)	203 (51)	
10,001-20,000	161(55)	134 (45)		92(59)	65 (41)	
$\geq$20,001	124(54)	106 (46)		46(57)	35(43)	
Education level			0.13			0.57
Junior high school	18(53)	16 (47)		5(38)	8(62)	
High school	164(49)	173 (51)		129(50)	127(50)	
Diploma/certificate	100(46)	119 (54)		101(53)	89(47)	
university	158(56)	126(44)		104(55)	85(45)	

Note. *May not total to N due to missing responses for some characteristics.

† χ^2 test comparing baseline characteristics between physician interview participants and non-participants for questionnaire self-reported cases

‡ χ^2 test comparing baseline characteristics between physician interview participants and non-participants for questionnaire self-reported non- cases

Table 2. Proportion of self-reported diabetes cases confirmed by physician interviews among participants according to baseline characteristics

Baseline characteristics	All cases interviewed n	All self-reported diabetes cases			Self-reported cases with T2DM		
		Cases confirmed during interview n	Percent of cases confirmed %	$P^{\dagger}$	Cases confirmed during interview n	Percent of cases confirmed %	$P^{\ddagger}$
Overall	442	364	82%		344	78%	
Sex				0.95			0.006
Males	282	232	82%		231	82%	
Females	160	132	83%		113	71%	
Age				0.13			0.001
Under 40	226	180	80%		162	72%	
40 or over	216	184	85%		182	84%	
Income				0.86			0.34
10000 and under	147	123	84%		110	75%	
10001- 20000	161	131	81%		125	78%	
20001 and over	124	103	83%		102	82%	
Education				0.78			0.21
Junior high school	18	15	83%		15	83%	
High school	164	137	84%		132	80%	
Diploma/certificate	100	84	84%		81	81%	
University degree	158	126	80%		114	72%	

Note. $^{\dagger}\chi^2$ test comparing the proportion of confirmed self-reported diabetes cases (type 2 diabetes and transient diabetes) by baseline socio-demographic characteristics.

$^{\ddagger}\chi^2$ test comparing the proportion of confirmed self-reported type 2 diabetes cases by baseline socio-demographic characteristics.

The findings from the logistic regression analyses are shown in Table 3. All of the self-reported non-cases correctly reported not having diabetes. Therefore, there was no variability in the socio-demographic characteristics associated with the correct reporting of diabetes status in this group. Among the confirmed self-reported T2DM diabetes cases, the adjusted model shows that female sex is associated with lower odds of agreement between the questionnaire and physician interviews (OR 0.5 (95% CI 0.3-0.9) and that older age is associated with higher odds of agreement between the questionnaire and physician interviews (OR 1.8 (95% CI 1.1-3.1). When the total group of confirmed self-reported diabetes cases (all types) was included, the association with sex was not apparent and was not statistically significant for age, indicating that these slight differences in the proportion of confirmed cases of T2DM may reflect the cases of gestational diabetes among the young women in this cohort.

Assessing validity of self-report according to sequential reporting pattern over the 2009 and 2013 follow-up surveys showed that the proportion of confirmed T2DM was highest among those who self-reported incident diabetes in both 2009 and 2013 96% (95% CI 93-99%), followed by those who reported incident diabetes only in 2013 86% (95% CI 81-91%), with the lowest proportion of confirmed T2DM cases being recorded among the participants who reported incident diabetes in 2009 and subsequently no diabetes in 2013 32% (95% CI 23-41%). The group of participants who reported incident diabetes in 2009 and subsequently reported no diabetes in 2013 had the largest proportion of the participants with transient diabetes in this cohort (16 of the total 20 participants with transient diabetes were in this reporting group).

Cumulative incidence of T2DM accounting for the effect of misclassification: Using self-reported questionnaire

data, the four-year cumulative incidence for T2DM from 2005 to 2009 in the TCS was 1.04% (95% CI 0.96-1.12%; 623/59,835). However, our physician interviews suggested that 29% of the group who reported diabetes in 2009, did not have T2DM. We applied this error to all of the 2009 self-reported cases and calculated a corrected estimate of the 2005 to 2009 four year T2DM cumulative incidence of 0.74% (95% CI 0.67-0.81%; 444/59,835). The 2009 to 2013 four-year cumulative incidence of T2DM based on self-report, was 1.05% (95% CI 0.97-1.13%; 411/39,220). For this reporting period our physician interviews indicated that, 14.4% of positive reporters did not have T2DM. By applying this T2DM reporting error to all of the 2013 self-reported cases we calculated a corrected estimate of the 2009 to 2013 four year T2DM cumulative incidence of 0.90% (95% CI 0.82-0.98%; 352/39,220). In a sensitivity analysis we additionally allowed the reporting error fractions to vary from 10-50% in the group lost to follow-up after 2009 and found that the four year 2005 to 2009 cumulative incidence estimates varied from 0.69% (95% CI 0.61-0.75%; 411/59,835) to 0.79% (95% CI 0.72-0.86%; 473/59,835).

Table 3. Associations between baseline characteristics and agreement between questionnaire data and interview findings for interviewed self-reported cases

N=442	**All self-reported diabetes cases** (Agreed cases n=364)				**Self-reported cases with type 2 diabetes** (Agreed cases n=344)			
	Crude		*Adjusted**		*Crude*		*Adjusted**	
Characteristics	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Sex								
Male sex	1		1		1		1	
Female sex	1.0	0.6-1.7	1.0	0.6-1.6	0.5	0.3-0.8	0.5	0.3-0.9
Age								
Age <40	1		1		1		1	
Age ≥40	1.5	0.9-2.4	1.5	0.9-2.7	2.1	1.3-3.4	1.8	1.1-3.1
Income per month								
≤ 10001	1		1		1		1	
10001-20000 baht	0.9	0.5-1.5	0.8	0.4-1.5	1.2	0.7-2.0	1.0	0.6-1.8
≥ 20001baht	1.0	0.5-1.8	0.8	0.4-1.7	1.6	0.9-2.8	1.1	0.5-2.3
Education								
High school	1		1		1		1	
Junior high	1.0	0.3-3.6	1.3	0.3-5.9	1.2	0.3-4.4	1.4	0.3-6.8
Diploma	1.0	0.5-2.0	1.1	0.6-2.3	1.0	0.5-1.9	1.2	0.6-2.4
University level	0.8	0.4-1.4	0.8	0.5-1.5	0.6	0.4-1.1	0.6	0.4-1.1

Note. * Results are adjusted for all variables included in the model

95% CI Confidence Intervals.

4. Discussion

This population-based study shows high validity of questionnaire self-reported doctor-diagnosed incident T2DM in younger and middle-aged Thai adults participating in a national cohort study. Using physician interviews as the gold standard, 78% of self-reported diabetes cases were confirmed as having diagnosed T2DM. Accuracy of self-report did not vary substantially by socio-demographic characteristics in this group of adult students. The proportion of confirmed self-reported cases was slightly lower among the young women in this cohort, a finding that is mostly likely attributed to transient diabetes. These findings highlight the need for cautious interpretation of self-reported diabetes data from a cohort with young women who may be reporting gestational diabetes rather than T2DM.

We also found that although questionnaire self-reports slightly over-estimated the cumulative incidence of T2DM over one wave of data collection, the misclassification of self-report became negligible once two waves of self-reported data were considered. Therefore, the repeated follow-up of self-reported data essentially eliminates the need for further validity testing of such individuals; a common finding when using repeated measures to assess the validity of self-report (Barr, Herbstman, Speizer, & Camargo, 2002).

This study has limitations that should be considered when interpreting the findings. Only 52% of the selected self-reported non-cases and 50% of the self-reported cases could be contacted by telephone. As such, those contacted may not be representative of the entire non-case and case group in the TCS and the validity of negative response might be lower than 100%. However, there were no significant differences in the socio-demographic characteristics of those interviewed and those who could not be contacted suggesting that the responses in the contacted group may be similar to those of the non-contactable group.

The method used to confirm self-reports in this study was physician telephone interviews, a method that may not be considered 'gold standard'. Accessing medical records, which may have been a better method of confirming doctor-diagnosed T2DM, was not feasible in this population due to the large-scale nature of this nationally dispersed cohort, and to time and cost constraints. However, the physician who conducted the interviews is an experienced clinician with local knowledge of diabetes diagnosis and treatment pathways so is likely to have elicited accurate histories of diabetes diagnoses.

There is an additional study consideration that should be emphasized. The questions in the surveys did not differentiate between type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus or transient (i.e. gestational or corticosteroid medication induced) diabetes. Therefore, it is possible that some of the self-reported incident diabetes cases may have had type 1 diabetes. However, this is unlikely because in this study we excluded prevalent (reported at baseline) cases of diabetes and the median age of this cohort was much higher than that at which T1DM is generally diagnosed.

Our investigations also do not reflect the likelihood that there are undiagnosed cases in this cohort and accordingly a higher incidence of T2DM among TCS participants. However this is unlikely to be a major problem since the participants are well educated and because diabetes awareness has received a great deal of attention in Thailand since the implementation of the national screening program and the national health coverage scheme in the past decade (Aekplakorn et al., 2011; Prakongsai, Limwattananon, & Tangcharoensathien, 2009).

The high proportion of validated self-reported cases and non-cases found in this study is similar to findings from studies conducted in health professional cohorts (Field et al., 2001; Hu et al., 2001) and is slightly higher than findings reported from two studies conducted among Asian populations (Goto et al., 2013; Wu, Li, & Ke, 2000). These differences might be explained by the differences in the characteristics of our study cohort, which was younger and/or had a higher education level than the cohorts sampled in other Asia-based studies (Goto et al., 2013); these characteristics have been shown to be associated with a higher accuracy of self-reporting diabetes in some prior research (Molenaar et al., 2007; Okura et al., 2004). The association between older age and the inaccurate reporting of chronic diseases has been attributed to declining cognitive function (Sherbourne & Meredith, 1992), and/or the reluctance of the elderly to admit or perceive that they have a chronic disease (Kriegsman, Penninx, Van Eijk, Boeke, & Deeg, 1996). Furthermore, among some Asian immigrant groups, younger age has been found to be associated with higher levels of formal education (Tseng, Halperin, Ritholz, & Hsu, 2013). Accordingly, the association between age and the inaccurate reporting of health status may partially be explained by education levels (Goldman et al., 2003). The proportion of validated self-reported cases in this study was slightly lower than findings from one study conducted in China. This may be due to the higher prevalence of diabetes in their older study cohort (Yuan et al., 2015).

Although the validity of self-reported doctor diagnosed diabetes in this study was high, these findings may be less applicable to the broader Thai population, which, on average, is older and has a lower education level than the Thai Cohort Study participants (A. C. Sleigh et al., 2008). Nonetheless, despite the differences in the cohort structures and gold standard methods used to validate self-reported diabetes in this study and among other validation studies, the general findings, from both Western populations conducted mostly with older and highly educated cohorts and Asian populations conducted mostly with younger and/or less educated cohorts, are that the validity of survey self-reported diabetes is generally high (Goldman et al., 2003; Huerta, Tormo, Egea-Caparrós, Ortolá-Devesa, & Navarro, 2009; Wu et al., 2000). Clearly, careful attention must be given to structuring the diagnostic questions, with specification of doctor-diagnosis and (if relevant) hospitalization having shown to be important for many diseases (Barr et al., 2002; Yuan et al., 2015).

Our study found that personal socio-demographic characteristics were not statistically significantly associated

with the validity of self-reported doctor diagnosed diabetes. The lack of significant differences in accuracy of reporting across personal characteristics and high overall agreement between questionnaire data and physician telephone interviews is likely due to the medical importance of this disease (Goldman et al., 2003). Diabetes requires ongoing regular medical treatment and engagement with medical professionals long after its diagnosis (Kehoe, Wu, Leske, & Chylack, 1994; Pastorino et al., 2014). Although conditions such as hypertension share some of these same medical qualities, the accuracy of survey self-reported hypertension is generally lower than the accuracy of survey self-reported diabetes. This may be because hypertension can be a less disabling disease than diabetes during everyday life, people who are controlling their hypertension may think that they no longer have the condition and may be less likely to report it (Molenaar et al., 2007). Furthermore, hypertension is not recognized as a chronic disease by some ethnic groups (Goldman et al., 2003).

Data from repeated measures showed that the proportion of confirmed survey self-reports was highest among the participants who self-reported the same diabetes status consistently at the two follow-up questionnaires. Conversely, the proportion of confirmed survey self-report was the lowest among the participants who self-reported incident diabetes in 2009 and subsequently self-reported not having diabetes in 2013. We found that over a third of these participants had transient diabetes (gestational or corticosteroid medication induced) in the first follow-up questionnaire and as such accurately reported not having diabetes in the second follow-up questionnaire. Although transient diabetes generally has a low prevalence in cohort studies, particularly in cohorts that are older than this one, using repeated measures was found to be a good tool for detecting the 'true' T2DM cases. Moreover, having a four year interval in between follow-ups enabled the identification of transient diabetes due to gestational diabetes.

Cumulative incidence estimates calculated using the questionnaire data and the physician interview-corrected data demonstrate that questionnaire self-report slightly over-estimated the cumulative incidence. Although this slight over-estimation should be taken into account when calculating T2DM incidence and its determinants in this cohort, it is likely to have minimal impact on relative risk measures (Copeland, Checkoway, McMichael, & Holbrook, 1977) (Rothman, Greenland, & Lash, 2008).

4.1 Conclusions

The current study demonstrates that the proportion of questionnaire self-reported doctor-diagnosed incident T2DM cases confirmed using physician interviews is high and that questionnaire T2DM self-report is a valid tool for detecting new cases of T2DM in a large Thai population-based study. These findings suggest that self-reported incident T2DM can be used to assess the trends and determinants of incident T2DM, particularly in younger and educated Thai adults.

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Competing Interests Statement

The authors declare that there are no conflicts of interest.

Ethics and Consent

Ethical approval was obtained from Sukhothai Thammathirat Open University Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocol 2004344, 2009570 and 2014/782).

Consent

The physician received verbal consent to publish all interview data from each interviewee prior to conducting the interview.

Authors' Contributions

KP devised the validation study, constructed the interview protocol, entered and analysed all of the data and wrote the paper. PT conducted the telephone interviews and assisted in the development of the interview protocol. SJ, CB and AS assisted with the planning of the study and its required analyses, with the development of the

interview protocol, with the interpretation of the study findings and with the editing of all drafts. CD guided the analytical approach of this paper, supervised all analyses of the data and helped with the interpretation of the study findings. AS and SS conceived and developed the cohort. All authors approved the final manuscript.

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4

INCIDENCE AND RISK FACTORS FOR TYPE 2 DIABETES IN THAI ADULTS

4 Incidence and risk factors for T2DM in Thai adults

Chapter 4 is a peer-reviewed article that has been published in the *BMJ Open*. It addresses Objective 2: to analyse the disease (T2DM) incidence and associated risks. Longitudinal data from the 2005, 2009, and 2013 TCS surveys were used to assess T2DM incidence and its potential risk factors in participants who were diabetes free at the start of the observation period in 2005 and followed up over the eight years (N=39,507). Results demonstrate and quantify the high incidence of T2DM and identify the various health-risk factors driving the T2DM epidemic in the Thai population. This information is significant for public policy and health planning.

BMJ Open

Incidence and risk factors for type 2 diabetes mellitus in transitional Thailand: results from the Thai cohort study

Keren Papier,[1,2] Susan Jordan,[2] Catherine D'Este,[1] Chris Bain,[1,2] Janya Peungson,[3] Cathy Banwell,[1] Vasoontara Yiengprugsawan,[1,4] Sam-ang Seubsman,[3] Adrian Sleigh[1]

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For numbered affiliations see end of article.

Correspondence to
Ms Keren Papier;
Keren.Papier@anu.edu.au

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is increasingly prevalent in countries undergoing rapid development, including Thailand. We assessed T2DM incidence over an 8-year period in a nationwide cohort of Thai adults.

Methods: Thai Cohort Study participants were surveyed in 2005, 2009 and 2013. The analysed cohort members were aged (15–88), did not have diabetes in 2005 and were followed up by questionnaire in 2013 (n=39 507). T2DM was ascertained using self-report, which has been validated using physician interviews. We calculated the 8-year cumulative incidence of T2DM. Multivariable logistic regression assessed associations between potential risk factors and T2DM incidence.

Results: 8-year cumulative incidence of T2DM (2005 to 2013) was 177 per 10 000 (95% CI 164 to 190). Crude and age-standardised cumulative incidences of T2DM by sex were 249 per 10 000 (95% CI 226 to 272) and 222 per 10 000 (95% CI 219 to 225) for men; and 119 per 10 000 (95% CI 105 to 133) and 96 per 10 000 (95% CI 94 to 98) for women, respectively. T2DM increased significantly for both sexes with increasing age and body mass index (BMI) (p trend <0.001 for both). Residence in an urban area as a child associated with T2DM among men and women (OR=1.4, 95% CI 1.1 to 1.7 and OR=1.4, 95% CI 1.01 to 1.79); this was no longer statistically significant after adjusting for BMI. Among men, smoking (OR=1.7, 95% CI 1.3 to 2.2) and alcohol intake (OR=1.8, 95% CI 1.1 to 3.0) were associated with T2DM.

Conclusions: This study found that the sociodemographic and lifestyle changes that have accompanied Thailand's economic development are associated with T2DM risk in a large cohort of Thai adults. Our findings highlight the need to address these transitions to prevent a further increase in the national incidence of T2DM, particularly among Thai men.

Strengths and limitations of this study

- This nationwide study is the largest longitudinal study of health-risk factors and diabetes risk in Thailand.
- The participants in our cohort reflect Thais well socioeconomically and geographically.
- All diabetes diagnoses rely on self-report.
- An issue in this study is the loss to follow-up of cohort participants over the 8-year period.

BACKGROUND

Rapid economic development accompanied by environmental, social and behavioural change occurred in many low and middle-income countries (LMICs) over the past few decades. Concomitant shifts in behaviours[1] led to a health-risk transition, including epidemiological and health transitions,[2 3] with falling infectious diseases, reduced childhood mortality and increases in non-communicable diseases such as type 2 diabetes mellitus (T2DM).[4]

Thailand is one such country with rapidly emerging T2DM. Its prevalence among adults has risen from 2.3% in 1991[5] to 8.0% in 2015.[6] Over 4 million Thai adults live with diabetes, making it the top cause of disability-adjusted life years lost for Thai women and the seventh cause for men.[7] T2DM is also an economic burden; in 2008 average annual cost per patient was US$ 881—21% of per capita gross domestic product.[8]

Causes of the diabetes epidemic in industrialised countries are reasonably well established,[9–11] but much less is known in LMICs such as Thailand. In developed countries, T2DM is inversely related with income and education while the opposite is usually noted when diabetes first emerges in LMICs.[12 13] How environmental, social and behavioural changes are affecting T2DM risk among Thais is not known. The first three studies that reported on diabetes in Thailand were

limited in size (under 7000 participants), location (Bangkok) or occupation (office workers, university employees or Electric Generation Authority plant workers).[14–16] Despite the restrictions, these studies produced new knowledge for Thailand on downstream (eg, age and body mass index (BMI)) risk factors for T2DM. Incidence rates were estimated but upstream risks (geographical, socioeconomic) were not reported and the studies could not investigate beyond Bangkok. Our study was designed to fill this gap, is not geographically or occupationally restricted and is large in size. Accordingly, information emerging has application to the wide population of Thailand and as well as most of Southeast Asia.

Here we report an 8-year prospective cohort study providing nationwide data on incidence of T2DM and its risk factors. This information should help identify prevention targets and reveal the current state of the health transition in Thai adults.

METHODS

Study population

The Thai Cohort Study (TCS) is a longitudinal study of distance learning Open University students. It was established to investigate how rapid socioeconomic development is affecting health behaviours and outcomes in Thailand—the health-risk transition.[3] In 2005, a 20-page questionnaire was mailed to all 200 000 students enrolled at Sukothai Thammithirat Open University. These students are generally adults of modest means using education for self-improvement; they are embedded in their communities nationwide and are expected to experience the health-risk transition ahead of their fellow Thais. The questionnaires were self-completed in 2005, 2009 and 2013. Items included socioeconomic, demographic, cultural and lifestyle characteristics, health-risk behaviours and self-reported health outcomes including diabetes.

Ascertainment of diabetes status

At each wave of data collection, participants were classified as having diabetes if they responded positively to the question ('Have you ever received a confirmed diagnosis from a doctor that you definitely have diabetes?'). We used telephone interviews undertaken by a practicing Thai physician to confirm the validity of a large proportion of questionnaire-reported doctor-diagnosed T2DM and transient diabetes. Type 2 diabetes status was determined by the physician based on the participants' answers to a standard interview protocol. The protocol was developed following the American Diabetes Association's classification guidelines for diagnosing diabetes.[17] The protocol included questions probing about blood sugar testing and cut-off criteria used for diagnosis, treatment and names of medications prescribed by the physician and about frequency of medical visits and the types of tests taken during medical visits. The validation study of these self-reported cases indicated high accuracy (78%), particularly among those (n=148) who reported doctor-diagnosed diabetes in 2009 and 2013 (96%) (*Unpublished data*).

Eligibility

Participants were included in the study if they reported that they did not have diabetes at baseline in 2005 and if they provided diabetes status in the 2013 questionnaire. Excluded were those reporting diabetes at baseline (prevalent cases), and those reporting diabetes in 2009 and then reporting no diabetes in 2013 (mostly women with gestational diabetes).

Assessment of risk factors

We assessed health, lifestyle and sociodemographic variables reported at baseline as potential risk factors for incident T2DM. The sociodemographic information included age, personal monthly income, highest education level and area of residence in childhood (urban or rural). Health and lifestyle information included fruit, vegetable, tobacco and alcohol consumption and weight and height.[18] For BMI, we divided weight in kilograms by height in m^2 and categorised as recommended for Asian populations.[19]

Incidental exercise was measured by frequency of 'housework or gardening'. 'Leisure physical activity' scored as adjusted number of sessions per week of strenuous, moderate or mild exercise ('2×strenuous +moderate+mild+walking' exercise sessions);[20 21] this weighted score was then categorised by sessions per week (none, 1–7, 8–14, 15 or more).

Statistical analysis

Cumulative incidence

We calculated 8-year cumulative incidences of T2DM. Denominators included all participants who recorded no diabetes in 2005 and reported their diabetes status in 2013; numerators included those reporting having T2DM in 2013. Eight-year cumulative incidences were also stratified by age and sex.[5] We also age-standardised the sex-specific rates to the WHO reference population for the year 2000.[22] We estimated age of onset as baseline age plus 2 years for those reporting T2DM in 2009 and baseline age plus 6 years for those reporting T2DM in 2013.

Risk factors for incident T2DM

We classified risk factors to be upstream (geographical, socioeconomic) or downstream (biomedical, personal). These different levels are important for designing the type of public health intervention. With T2DM as the outcome (yes/no), we used logistic regression to estimate ORs and 95% CIs for baseline risk factors.

Women in the cohort were, on average, younger than the men with 51% of women aged <30 at baseline versus 36% of men. Owing to the different age distributions and the potential for different associations by sex, all

analyses were stratified by sex and adjusted for age. We used three models of increasing complexity. This enabled us to assess risk factors for T2DM with and without the impact of BMI, an important risk factor for T2DM.[23] The first model (Model 1) had eight variants. One variant included age alone; the other seven variants each included one other risk factor of interest. The second model (Model 2) included all of the risk factors except for BMI. The third model (Model 3) included all risk factors and BMI. All analyses were carried out using Stata (V.13.0). A two-sided significance level of 0.05 was used.

Sensitivity analysis

We undertook two sensitivity analyses. For the first sensitivity analysis, we calculated the 4-year incidence of T2DM within each 4-year follow-up (2005 to 2009; 2009 to 2013) to determine whether the cumulative incidence estimates derived from these two 4-year periods were consistent with findings from the 8-year period (2005 to 2013).

In the second sensitivity analysis, we examined risk factors associated with T2DM incidence in the first 4 years (2005 to 2009) for four different subgroups: (1) everyone reporting incident T2DM in 2009; (2) excluding those reporting diabetes in 2009 but not in 2013; (3) excluding those lost to follow-up in 2013 and (4) only including those reporting T2DM in 2009 and 2013. Risk factor patterns for the four subgroups were compared with patterns for the 8-year results, assessing the effect of selection and information bias (attrition and misclassification).

Informed written consent was obtained from all participants. All data were de-identified before analysis.

RESULTS

Participants

The study population included TCS members who had been followed from 2005 to 2013, excluding 902 who reported diabetes at baseline and 167 who reported having diabetes in 2009 and not having diabetes in 2013, most being young women with transient (gestational) diabetes. Of the 39 507, the remaining cohort members initially at risk—698 reported being diagnosed with T2DM (figure 1).

The median (first and third quartiles) for age in years at baseline were 38 (32, 44) for those reporting T2DM and 31 (26, 37) for those who did not.

Cumulative incidence of T2DM from 2005 to 2013

Between 2005 and 2013, the overall T2DM cumulative incidence was 177 per 10 000 (95% CI 164 to 190). Corresponding crude and age-standardised cumulative incidences by sex were respectively: for the 17 607 men, 249 per 10 000 (95% CI 226 to 272) and 222 per 10 000 (95% CI 219 to 225); for the 21 900 women, 119 per 10 000 (95% CI 105 to 133) and 96 per 10 000 (95% CI 94 to 98). Figure 2 shows the age–sex-specific cumulative incidences of T2DM between 2005 and 2013. The incidence rose with age for both sexes, almost exponentially for men from age 50.

Risk factors for incident T2DM

Upstream risk factors

For men, high income (≥20 000 Baht per month) compared with low income (10 000 Baht per month or less) and tertiary education relative to high school or less education statistically associated with T2DM in the models adjusted for age (Model 1) but not in the models adjusted for other risk factors (Models 2 and 3). There was no statistically significant association between T2DM and either income or education for women. For both sexes, there was a modest relationship with having lived in an urban area between the ages of 10 and 12 in Models 1 and 2 (Model 2:men OR=1.4, (95% CI 1.1 to 1.7); women OR=1.4, (95% CI 1.01 to 1.79)), but after adjustment for BMI (Model 3), the magnitude of the effect estimates for urban residence approached unity, falling by 14% for men and 21% for women and were no longer statistically significant (table 1).

Downstream risk factors

Infrequent gardening or housework associated with significantly increased odds of T2DM for men in Model 1 only. In Model 2, for men and women, age was associated with T2DM (≥50 years: OR=9.0, (95% CI 5.8 to 14.0) and OR=9.9, (95% CI 5.2 to 19.0), respectively). Obesity (BMI≥30.0 kg/m^2) was associated with significantly increased odds of T2DM incidence in men (OR=23.1, 95% CI 16.1 to 33.0) and women (OR=28.5, 95% CI 18.7 to 43.4), respectively (Model 3). Among men, regular alcohol intake (OR=1.8, (95% CI 1.1 to 3.0)) and current smoking (OR=1.7, (95% CI 1.3 to 2.2)) also associated with increased T2DM risk (Model 3). Addition of BMI to the models substantially attenuated OR estimates for age (32% for men, 48% for women aged ≥50 years) but had little influence on ORs for smoking, or alcohol (table 1).

Sensitivity analysis

Incidence across the two 4-year periods was stable—104 per 10 000 (95% CI 96 to 112) (2005 to 2009) and 105 per 10 000 (95% CI 95 to 115) (2009 to 2013). The cumulative incidence of T2DM per 10 000 in men was approximately double that in women across the two 4-year periods (period 1:146 vs 70; period 2:146 vs 72). The findings from the two 4-year periods are consistent with those from the 8-year period (see online supplement 1).

The 2005 to 2009 4-year risk factor effect estimates were similar across the different subgroups (see Methods). An example from findings for men is shown in figure 3. Neither attrition nor accuracy of T2DM self-report had an impact on the 8-year risk analyses.

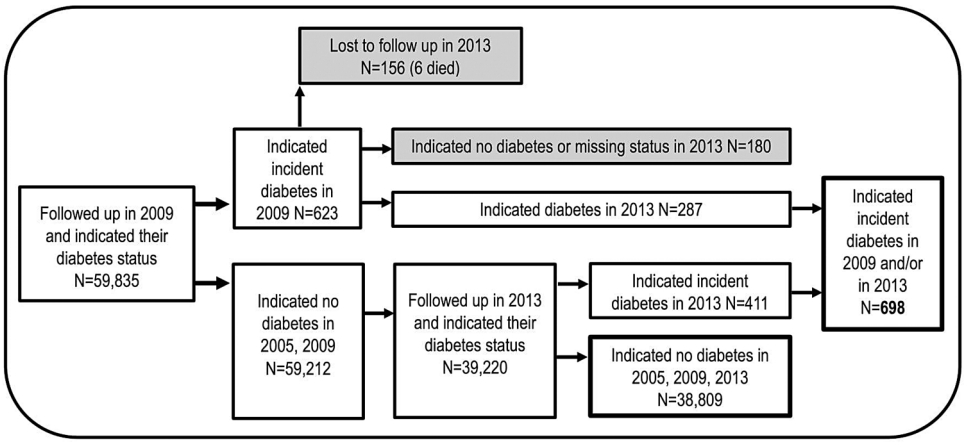

Figure 1 Selection of study participants from the Thai Cohort Study. *Participants were selected based on self-reported diabetes status in 2005 and available follow-up data in 2009 and 2013. The self-reported positives in 2005 were excluded (n=902) as were those missing in 2009 and those with a missing diabetes status in their questionnaires. Eight-year cumulative incidence was calculated with the 39 507 remaining participants in 2013.

DISCUSSION

We assessed factors associated with incidence of T2DM over 8 years in a nationwide cohort of young and middle-aged Thai adults. The 8-year cumulative incidence of T2DM between 2005 and 2013 was 177 per 10 000 (95% CI 164 to 190). T2DM incidence was higher among men (249 per 10 000; 95% CI 226 to 272) than women (119 per 10 000; 95% CI 105 to 133). For both sexes, factors most strongly associated with odds of developing T2DM were increasing age and higher BMI. Living in an urban area during childhood, smoking and alcohol are associated with increased risk of T2DM among men. However, most upstream associations attenuated when BMI was added to models. Tertiary education was associated with a small decrease in T2DM risk among women but this was not statistically significant.

There are limitations when interpreting these findings. All diabetes diagnoses used self-report so there may be case classification error. However, a validation study of self-reported diabetes conducted among TCS participants indicated that accuracy of T2DM self-report was high. Also an issue is loss to follow-up. Overall, about 50% of the baseline cohort was retained after 8 years. A similar retention rate was noted for all values of sex, fruit, vegetable and alcohol intake and area of residence indicating that attrition for these variables should not be a concern.[24] However, differential attrition was noted for the youngest age group, those underweight and those with the lowest income or lowest education and those who reported smoking in 2005. Differential attrition of participants who smoke might lead to an underestimation of T2DM incidence but differential retention of participants who are older and have a larger body size might lead to an overestimation of T2DM incidence. However, results in the first 4 years (70% of baseline cohort) showed similar results to the total 8 years giving us confidence in generalisable findings.

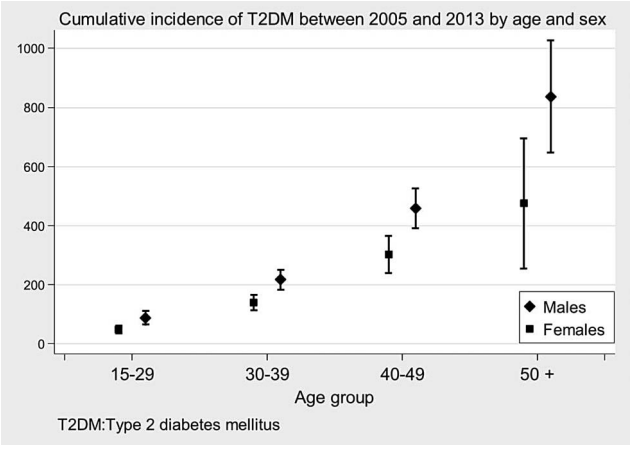

Figure 2 Cumulative incidence of T2DM between 2005 and 2013 by age and sex.

This study has several strengths, including size, nationwide coverage and prospective longitudinal design. However, compared with the Thai population our cohort is younger, has higher levels of education and includes a higher proportion of adults living in metropolitan Bangkok.[3] Incidence estimated by our study may be higher or lower than in the general population but the age-specific rates we report are expected to be generalisable, at least for educated groups. Furthermore, the participants in this cohort are ideal for studying the effects of sociodemographic change on T2DM risk since they are Thais of modest means, embedded in geographically dispersed communities across the nation and self-improving via education. Our population has been most informative and clearly represents well the large segment of the Thai population now entering the transition through a modern set of health concerns having undergone great changes in the environment, diet and lifestyle.[3] We expect them to undergo the 'health-risk transition' ahead of fellow Thais.[25 26]

Table 1 Associations between baseline characteristics and 8-year cumulative incidence of diabetes (2005 to 2013), Thai Cohort Study

Baseline characteristics	Diabetes status in 2013		Men N=17 607 * OR (95% CI)			Women N=21 900 * OR (95% CI)		
	Incident cases	Total at risk	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Age	n (%)	N=39 507 *						
15–29	108 (1.0)	17 447	1	1	1	1	1	1
30–39	252 (2.0)	14 383	2.5 (1.8 to 3.4)	2.4 (1.7 to 3.4)	2.0 (1.4 to 2.8)	2.9 (2.1 to 4.1)	2.8 (1.9 to 4.1)	2.1 (1.4 to 3.0)
40–49	253 (4.0)	6506	5.4 (4.0 to 7.4)	4.7 (3.3 to 6.8)	3.4 (2.3 to 5.0)	6.5 (4.6 to 9.2)	6.3 (4.1 to 9.6)	3.8 (2.4 to 5.9)
50 and over	85 (7.0)	1171	10.4 (7.2 to 14.9)	9.0 (5.8 to 14.0)	6.1 (3.9 to 9.7)	10.4 (6.0 to 18.2)	9.9 (5.2 to 19.0)	5.1 (2.6 to 10.0)
Income(Baht/month)								
<10 000	267 (1.0)	22 926	1	1	1	1	1	1
10 001–20 000	227 (2.0)	10 928	1.1 (0.9 to 1.4)	1.0 (0.7 to 1.2)	0.9 (0.7 to 1.1)	1.0 (0.7 to 1.3)	1.0 (0.7 to 1.4)	1.0 (0.7 to 1.5)
>20 001	188 (4.0)	4907	1.3 (1.00 to 1.72)	1.1 (0.8 to 1.5)	1.1 (0.8 to 1.4)	1.0 (0.7 to 1.5)	0.9 (0.6 to 1.4)	1.1 (0.7 to 1.7)
Education								
High school or less	298 (2.0)	17 084	1	1	1	1	1	1
Tertiary education	396 (2.0)	22 328	1.2 (1.00 to 1.47)	1.1 (0.9 to 1.4)	1.1 (0.9 to 1.3)	1.0 (0.8 to 1.3)	0.9 (0.7 to 1.2)	0.9 (0.7 to 1.2)
Childhood area of residence								
Countryside (rural)	448 (2.0)	29 248	1	1	1	1	1	1
City/town (urban)	237 (2.0)	9891	1.5 (1.2 to 1.9)	1.4 (1.1 to 1.7)	1.2 (0.9 to 1.5)	1.3 (1.0 to 1.7)	1.4 (1.01 to 1.79)	1.1 (0.8 to 1.4)
BMI (kg/m^2) *(Asian cut points)*								
Underweight ≤18.49	8 (0.2)	5183	0.8 (0.3 to 1.9)		0.7 (0.3 to 2.0)	0.2 (0.1 to 0.7)		0.2 (0.1 to 0.8)
Normal (18.5–22.9)	123 (1.0)	20 997	1		1	1		1
At risk (23.0–24.9)	121 (2.0)	6381	1.8 (1.3 to 2.6)		1.9 (1.4 to 2.8)	3.6 (2.4 to 5.3)		3.7 (2.4 to 5.7)
Obese I (25.00–29.9)	294 (5.0)	5489	5.1 (3.9 to 6.8)		5.4 (3.9 to 7.3)	10.1 (7.2 to 14.2)		10.4 (7.2 to 15.0)
Obese II (≥30.0)	142 (15.0)	971	20.6 (14.7 to 28.9)		23.1 (16.1 to 33.0)	27.7 (18.8 to 40.8)		28.5 (18.7 to 43.4)
Gardening or housework								
Most days	362 (2.0)	22 010	1	1	1	1	1	1
1–2 times/week	176 (2.0)	10 617	1.0 (0.8 to 1.3)	1.0 (0.8 to 1.3)	0.9 (0.7 to 1.2)	1.2 (0.9 to 1.6)	1.2 (0.9 to 1.7)	1.3 (0.95 to 1.80)
≤3 times a month	148 (2.0)	6429	1.3 (1.0 to 1.7)	1.2 (0.9 to 1.5)	1.0 (0.8 to 1.3)	1.3 (0.9 to 1.8)	1.1 (0.7 to 1.7)	1.0 (0.7 to 1.6)
Smoking								
Never smoked	384 (1.0)	28 632	1	1	1	1	1	1
Ex-smoker	157 (3.0)	6128	1.1 (0. 9 to 1.4)	1.1 (0.8 to 1.4)	1.0 (0.7 to 1.3)	0.7 (0.3 to 1.6)	0.8 (0.4 to 1.9)	0.6 (0.2 to 1.5)
Current smoker	119 (4.0)	3173	1.9 (1.5 to 2.4)	1.7 (1.3 to 2.2)	1.7 (1.3 to 2.2)	2.1 (0.8 to 5.9)	1.7 (0.5 to 5.6)	1.1 (0.3 to 4.0)
Alcohol intake								
Never	152 (1.0)	10 873	1	1	1	1	1	1
Used to drink (quit)	71 (2.0)	3252	1.5 (0.97 to 2.42)	1.5 (0.9 to 2.5)	1.7 (1.0 to 2.9)	0.6 (0.3 to 1.1)	0.6 (0.3 to 1.2)	0.6 (0.3 to 1.2)
Occasional/social	399 (2.0)	23 049	1.4 (0.9 to 2.0)	1.4 (0.9 to 2.1)	1.5 (0.96 to 2.37)	0.9 (0.7 to 1.1)	0.9 (0.7 to 1.2)	0.9 (0.2 to 1.3)
Regular drinker	68 (4.0)	1900	2.0 (1.3 to 3.1)	1.7 (1.00 to 2.77)	1.8 (1.1 to 3.0)	0.5 (0.1 to 3.9)	0.5 (0.1 to 3.9)	0.7 (0.1 to 5.2)

Model 1, age adjusted; Model 2, age and all variables except BMI; Model 3, Model 2 with BMI.
*Numbers may not add to total sample size due to missing responses for some characteristics.

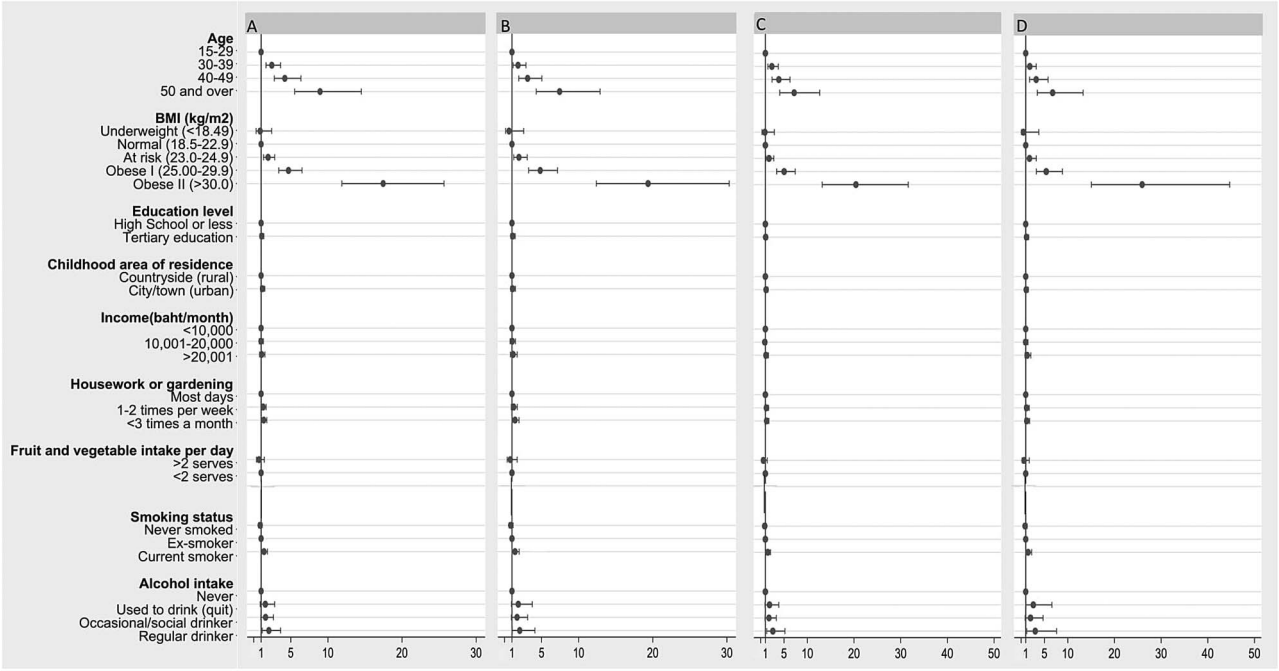

Figure 3 Sensitivity analysis comparing the ORs for incidence of diabetes between 2005 and 2009 according to diabetes reporting pattern in 2009 and 2013. Models were run for 4-year cumulative incidence between 2005 and 2009 among men, including the following participants. (A) Including all male participants followed up in 2009 (n=26 885). (B) Excluding the 107 male participants who reported having incident diabetes in 2009 but subsequently reported not having diabetes in 2013 (n=26 778). (C) Excluding the 7949 male participants who were lost to follow-up in 2013 (n=18 936). (D) Excluding the 7949 male participants who were lost to follow-up in 2013 and the 107 male participants who reported having incident diabetes in 2009 but subsequently reported not having diabetes in 2013 (n=18 829).

The sex and age-specific cumulative incidence of T2DM between 2005 and 2013 was comparable with findings reported by previous Thai studies.[14–16] Furthermore, our sex and age-specific estimates suggest that the incidence of T2DM among Thai cohort members is higher than Caucasian counterparts from North America[27] and Europe;[28] similar to Bangladesh,[29] and China;[30] and lower than Pima Indians[31] and Mauritians.[32] However, direct comparisons are difficult due to differences in the case ascertainment, attrition and population sampling.

In the TCS, increasing age and BMI were the strongest risk factors for T2DM. Increasing age is a well-known risk for T2DM[6 19] and its effects were very apparent in this relatively young cohort. The high rates of T2DM incidence in our cohort members is consistent with findings from studies with Asian populations that have also shown that the risk of T2DM starts to increase at a relatively low age in Asian populations.[33 34] The association with BMI is not surprising given that obesity is a well-established cause of diabetes.[10 35] Fat cells secrete hormones and adipokines that can increase the risk of diabetes through several pathways, including the increase in insulin resistance.[36] However, there are some notable differences between our findings and those from studies conducted in Caucasian populations. The incidence of T2DM in those with a BMI in the range of 23–24.9 kg/m^2 (healthy weight in Caucasians)[37 38] was equivalent to the incidence rate of T2DM reported at higher BMI levels of 30.0 kg/m^2 in Caucasians.[19 38] Our finding is consistent with findings from other Asian populations that have also shown that the risk of T2DM starts to increase at relatively low levels of BMI.[33] T2DM and body size relations in Thai adults need further research.

Urbanisation accompanies socioeconomic growth in developing countries.[39] We found that living in an urban area as a child increased risk of T2DM among men and women in models without adjustment for BMI. Previous reports from this cohort[40] and other developing countries[12] shows urbanisation is associated with reduced physical activity, increased consumption of alcohol and highly processed food items and a higher BMI level. The attenuation of the association between urbanisation and T2DM risk that we observed after the addition of BMI to our model suggests that BMI has a major impact on the relationship between urbanisation and T2DM.

We found a 'developing country' pattern of increasing T2DM along with higher income and education for men (but not for women) in age-only adjusted models. The income and education effect were attenuated in the fully adjusted model. Other LMICs have shown that higher levels of education or socioeconomic status (SES) have a direct relationship with T2DM risk, whereas the opposite has been shown in developed western countries.[13] However, once a country enters an advanced stage of economic development (equivalent to a gross national product per capita of around US$

2500), the prevalence of obesity begins to rise predominantly in the group with the lowest SES and education level[13 41 42] and women are the first to manifest an inverse relationship between SES and obesity risk.[41] Similar shifts appear to be occurring in the TCS cohort.[43] Thus, our results suggest that women, at least in this cohort, are at a more advanced stage of the health transition. These findings highlight the need for public health interventions to target the risk factors for T2DM differently in men and women.

Men in this cohort are taking more health risks (smoking, regularly consuming alcohol and being less physically active) than the women[44] and these risks link to T2DM. Public health efforts should preserve and encourage the low rates of alcohol consumption and smoking in Thai women to ensure that they do not adopt these new lifestyle behaviours, which lead to increased weight gain, insulin resistance and poor cardiovascular health.[45] Concomitantly, the cessation of alcohol intake and smoking should be promoted among Thai men.

CONCLUSION

This study presents the 8-year cumulative incidence of T2DM between 2005 and 2013 and associated risk factors in a large cohort of Thai adults. We found that the incidence of T2DM was higher in men and that the lifestyle and sociodemographic changes that have accompanied Thailand's socioeconomic development are associated with T2DM risk. Thai men are likely to be in the middle stages of the health transition while women are more advanced. The focus of public health efforts should be on obesity, smoking and alcohol, particularly among men. The incidence of T2DM in Thailand is already high and many risks are converging especially obesity, ageing and physical inactivity. So we can expect T2DM will increase in importance rapidly over the next 1–2 decades and our data provide useful foresight regarding the growing impact of these changing risks.

Author affiliations
[1]National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, Australia
[2]Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane, Australia
[3]Thai Health-Risk Transition Study, School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi, Thailand
[4]Health and Wellbeing and Department of Global Health, Centre for Research on Ageing, Research School of Population Health, The Australian National University, Canberra, Australian Capital Territory, Australia

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Contributors KP devised the study, analysed all of the data and wrote the paper. SJ, CBain and AS assisted with the planning of the study and its required analyses, with the interpretation of the study findings and with the editing of all drafts. CD'E guided the analytical approach of this paper, supervised all analyses of the data and helped with the interpretation of the study findings. CBanwell, VY and JP assisted with the collection of the cohort data and with the editing of the manuscript. AS and SS conceived and developed the cohort. All authors approved the final manuscript.

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Supplement 1: Four-year cumulative incidence of T2DM (2005 to 2009; and 2009 to 2013) by sex and age

	Between 2005 and 2009					Between 2009 and 2013				
	Age * (years)	New cases	Total at risk	Cumulative incidence Per 10,000	95% CI	Age ** (years)	New cases	Total at risk	Cumulative incidence Per 10,000	95% CI
Men	<30	39	10,463	37	25-49	<30	14	3,113	45	21-69
	30-39	135	10,149	133	111-155	30-39	74	7,509	99	77-121
	40-49	148	5,095	290	244-336	40-49	104	5,031	207	168-246
	≥50	71	1,178	602	466-738	≥50	63	1,771	356	270-442
	Overall	393	26,885	146	132-160	***Overall***	255	17,424	146	128-164
Women	<30	64	18,115	35	26-44	<30	18	6,515	28	15-41
	30-39	87	10,564	82	65-99	30-39	57	9,469	60	44-76
	40-49	64	3,788	169	128-210	40-49	58	4,879	119	89-149
	≥50	15	483	311	156-466	≥50	23	933	247	147-347
	Overall	230	32,950	70	61-79	***Overall***	156	21,796	72	61-83
Total	<30	103	28,578	36	29-43	<30	32	9,628	33	22-44
	30-39	222	20,713	107	93-121	30-39	131	16,978	77	64-90
	40-49	212	8,883	239	207-271	40-49	162	9,910	163	138-188
	≥50	86	1,661	518	411-625	≥50	86	2,704	318	252-384
	Overall	623	59,835	104	96-112	***Overall***	411	39,220	105	95-115

* Based on age in 2005

** Based on age in 2009

5

SUGAR-SWEETENED BEVERAGE INTAKE AND TYPE 2 DIABETES RISK IN THAI ADULTS

5 Sugar-sweetened beverage and T2DM risk in Thai adults

Chapter 5 is a peer-reviewed article that has been published in *Nutrition & Diabetes*. It addresses Objective 3: to assess the direct and obesity-mediated diabetes effects of sugar-sweetened beverages. Longitudinal TCS data from the 2005, 2009, and 2013 surveys were used to assess direct and obesity-mediated associations between SSB consumption in 2005 and T2DM outcome in 2013. Participants were those who were diabetes free in 2005, consumed SSBs in 2005, and were followed up over the eight-year period (N=39,175). Results reported here demonstrate that SSB consumption increases T2DM risk in Thai adults independently of weight gain and obesity. This information provides local evidence that SSBs are an ideal target for public health interventions and guides public health efforts aimed at preventing increasing T2DM incidence in Southeast Asian populations.

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ORIGINAL ARTICLE

Consumption of sugar-sweetened beverages and type 2 diabetes incidence in Thai adults: results from an 8-year prospective study

K Papier[1,2], C D'Este[1], C Bain[1,2], C Banwell[1], S Seubsman[3], A Sleigh[1] and S Jordan[2,4]

BACKGROUND: The global prevalence of type 2 diabetes mellitus (T2DM) is high and is increasing in countries undergoing rapid socio-economic development, including Thailand. Sugar-sweetened beverage (SSB) intake may contribute to the risk of developing T2DM. However, few studies have assessed this association in Asian populations, and the results have been inconsistent. We aimed to assess that association in a prospective study of Thai adults.

METHODS: Data were from Thai Cohort Study participants surveyed in 2005, 2009 and 2013. The nation-wide sample included adult cohort members who were free of diabetes in 2005 and who were followed-up in 2013 ($n = 39\,175$). We used multivariable logistic regression to assess associations between SSB intake and eight-year T2DM incidence. We used a counterfactual mediation analysis to explore potential mediation of the SSB intake and T2DM-risk relationship.

RESULTS: In women (but not men) consuming SSBs once or more per day (versus rarely) was associated with increased T2DM incidence at the 8-year follow-up (odds ratio (OR) = 2.4, 95% confidence interval (CI) 1.5–3.9). Obesity in 2009 was found to mediate ~23% of the total association between SSB intake in 2005 and T2DM risk in 2013 (natural indirect effect 1.15, 95% CI (1.02, 1.31).

CONCLUSIONS: Frequent SSB consumption associated with higher T2DM incidence in women but not men. We found that a moderate proportion of the SSB-T2DM relationship was mediated through body mass index (BMI). Our findings suggest that targeting SSB consumption can help prevent a national rise in the incidence of T2DM.

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INTRODUCTION

Many low and middle income countries (LMICs) have experienced considerable social and economic development in recent decades inducing a 'health-risk transition' characterized by changes in environment, health behaviour and emergence of non-communicable diseases such as type 2 diabetes mellitus (T2DM).[1,2] Thailand is one such country that has experienced an increase in T2DM prevalence from 2.3% in1991[(ref. 3)] to 8.0% in 2015.[2]

Increasing sugar consumption in Thailand may relate to increased T2DM. Between 1983 and 2009 sugar consumption jumped from 12.7 to 31.2 kg per person per year,[4] much in carbonated soft drinks.[5] The 2009 National Health Examination Survey (NHES) shows that frequency of approximately daily intake of carbonated soft drinks doubled (from 7.9 to >16%) among Thais aged 15 years or older since 2003.[6]

Sugar-sweetened beverage (SSB) consumption, which includes sweetened carbonated soft drinks, has been linked to increased T2DM risk in African and Caucasian populations,[7–9] with some research suggesting the association is mostly mediated by increasing body mass index (BMI).[10,11] There are limited and inconsistent data on SSB consumption and T2DM risk among Asian populations.[12–14]

SSBs are an ideal target for public health interventions to help control the T2DM epidemic since they have no nutritional value, are not rooted in Thai culinary culture, and do not protect against disease.[15] Furthermore, past performance of the Thai government in banning tobacco promotion suggests that parallel approaches to controlling SSBs would be possible.[16] The aims of this study were to clarify the association between SSB consumption and T2DM risk over an 8-year period and whether they are mediated by BMI in a prospective study of Thai adults, the Thai Cohort Study.

SUBJECTS AND METHODS

Study population

The Thai Cohort Study (TCS) is a prospective study of 87 151 Thai adults enrolled at Sukothai Thammithirat Open University (STOU), established to examine the 'health-risk transition' in Thailand.[17] In 2005 all 200 000 students enrolled at STOU were mailed a questionnaire covering socio-demographic, health and lifestyle factors, and health outcomes (including diabetes). Overall 87 151 (44%) students returned the completed questionnaires forming the baseline cohort. Follow-up questionnaires were sent in 2009 and 2013 and respectively 60 569 (70% response rate) and 42 785 (71% of 2009 participants) were returned.

Eligibility. Participants were eligible for this study if they reported that they did not have diabetes at baseline, had a valid SSB intake response in 2005, and provided a diabetes status in 2009 and/or 2013.

[1]National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, Australia; [2]Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia; [3]Thai Health-Risk Transition Study, School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi, Thailand and [4]The School of Public Health, The University of Queensland, Brisbane Queensland, Australia. Correspondence: K Papier, National Centre for Epidemiology & Population Health, The Australian National University, Building 62, Mills Road, Canberra, Australian Capital Territory, 2601, Australia.
E-mail: Keren.Papier@anu.edu.au
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Assessment of T2DM status. Participants were classified as having diabetes if they responded positively to the question 'Have you ever received a confirmed diagnosis from a doctor that you definitely have diabetes?' by 2013. A validation study of self-reported diabetes conducted among TCS participants indicated that the accuracy of diabetes self-report was high (82%).[18]

Assessment of SSB intake. In each questionnaire participants were asked about their SSB consumption. In Thai, this translated to any carbonated sweetened beverage or soda and did not distinguish between regular and diet soda intakes. However, for consistency with previous TCS work[19] and the literature, we use the term SSBs throughout. SSB consumption at baseline was reported in categories and classified as: <1 weekly, 1 to 6 per week, or $\geqslant 1$ per day.

Assessment of covariates. Questionnaire items included sociodemographic characteristics: age, income, education level, and area of residence (urban/rural); lifestyle factors: smoking (never smoked, ex-smoker and current smoker) and alcohol consumption (never, ex-drinker, occasional/social drinker and regular drinker); fruit and vegetable consumption (categorized as <2 or $\geqslant 2$ serves/per day), and consumption of deep-fried food ($<3\times$ per month, 1–6 per week, 1+ per day). Leisure physical activity, reported as number of sessions per week of strenuous, moderate or mild exercise, was weighted ('$2\times$strenuous+moderate+mild+walking' exercise sessions)[20] and categorized by sessions per week (none, 1–7, 8–14, 15 or more).[21] Participants also reported height and weight. Body mass index (BMI—weight in kg divided by height in m^2) was categorized as recommended for Asian populations.[22] The questionnaires also asked about health conditions.

Statistical analysis

Since some diabetes risk factors may be sex-specific, we conducted all analyses separately for men and women.[12] Baseline characteristics of eligible participants were compared across the groups of SSB consumption.

We used logistic regression to assess the association between baseline SSB consumption and development of T2DM by 2013. We estimated age-adjusted odds ratios (OR) and 95% confidence intervals (CI) (model 1) and then selected variables to include in the fully-adjusted model using directed acyclic graphs (DAGs), based on the previous work with this cohort. These included age, area of residence, education, income, physical activity, consumption of fruit/vegetables, deep-fried food and alcohol, smoking, hypertension at baseline, and baseline BMI (model 2) (shown to be related to SSBs in our data[19]). We also assessed whether other variables potentially associated with an unhealthy lifestyle, (including western-style fast food intake, screen time, and other forms of sedentary behaviour) confounded that SSB-T2DM association. We found that inclusion of these factors in our models did not confound the association between SSB intake and T2DM incidence and therefore did not include these variables in our final analyses.

As it has been suggested that the relationship between SSB consumption and T2DM risk could vary by age and BMI[23] we stratified the models by baseline BMI (<25 versus $\geqslant 25$ kg m^{-2}) and age (<40 versus $\geqslant 40$ years). We also added the interaction terms of interest (SSB intake $\times$ age or SSB intake $\times$ BMI) to the main model.

We calculated population attributable fractions separately for men and women using the standard formula PAF = [(Incidence in total population − Incidence in unexposed)/Incidence in total population] $\times$ 100 to determine the proportion of T2DM in the population that could have been prevented if no-one had consumed SSBs daily. We used SSB intake at baseline as our exposure measure and calculated cumulative incidence by dividing the new cases of T2DM between 2005 and 2013 by those at risk in 2005.[24] We then multiplied the sex-specific 8-year cumulative incidence and the PAFs from our study by the total number of men and women in the national Thai population and divided by eight to estimate the number of T2DM cases in the national Thai population that might have been prevented annually if daily SSB consumption was avoided.

Mediation of incident T2DM in 2013 by obesity in 2009. We conducted mediation analyses to assess the extent to which obesity in 2009 mediated the effect of SSB intake in 2005 on T2DM risk in 2013.[10,11] For direct comparison with previous studies we estimated the ORs and 95% CI, adjusting for covariates from the main regression model with and without BMI in 2009. To avoid mediator-outcome confounding[25] we excluded participants who reported incident T2DM in 2009 from these analyses.

We also ran a counterfactual-based mediation analysis using Stata PARAMED,[26] which compares two regression models: the first model regresses the outcome (T2DM incidence) on the main exposure (SSB intake), the proposed mediator (obesity) and specified covariates; the second model regresses the proposed mediator (obesity) on the exposure variable (SSB intake) and specified covariates.[25]

The mediation analysis was carried out using logistic regression since the outcome (T2DM in 2013) is binary. We dichotomized SSB intake in 2005 (main exposure) into daily intake (1+ per day) versus non-daily intake, and BMI in 2009 (our proposed mediator) into $\geqslant 25$ versus <25 kg m^2. Covariates from the main logistic regression models were included, and an exposure mediator interaction to account for any interaction effect.[25]

We estimated the natural direct effect of SSB intake on T2DM risk and the natural indirect effect of SSB intake on T2DM risk mediated by obesity by fitting two logistic regression models; one for T2DM, conditional on SSB intake, BMI in 2009, SSB-obesity interaction, and relevant confounders; and one for obesity in 2009, conditional on SSB intake and relevant confounders. Using these two regression models we then derived the ORs for the natural direct effect of SSB intake on T2DM risk (Figures 1a–c) and the natural indirect effect mediated by obesity in 2009 (Figures 1a–c). The total effect was derived from the product of the natural direct and indirect effect. We also divided the natural logarithm of the natural indirect effect by the natural logarithm of the total effect to determine the proportion of the total association between SSB intake in 2005 and T2DM risk in 2013 mediated by obesity in 2009.

Sensitivity analysis

It has been suggested that measures of central adiposity (including waist circumference and waist-to-height ratio) may be more informative for assessing the impact of obesity on cardio-metabolic diseases like diabetes in Asian populations.[27,28] Therefore, we conducted analyses to assess mediation of the SSB-T2DM association by each of: a) 2005–2009 weight gain; b) 2009 waist circumference;c) 2009 waist-to-height ratio; and d) various binary BMI cut-points (overweight ($\geqslant 23$ versus <23 kg m^2), obese I ($\geqslant 25$ versus <25 kg m^2), and obese II ($\geqslant 30$ versus <30 kg m^2)).

We also examined the association between SSB intake at baseline and the development of incident T2DM reported in 2009 to enable investigation of effects of attrition between 2009 and 2013.

All analyses were carried out using Stata (version 13.0, Australian National University, Canberra, ACT, Australia). All statistical tests were two-sided.

Ethical approval for the study was obtained from STOU Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocols 2004/344, 2009-/570). All participants gave informed written consent and data were de-identified before analysis.

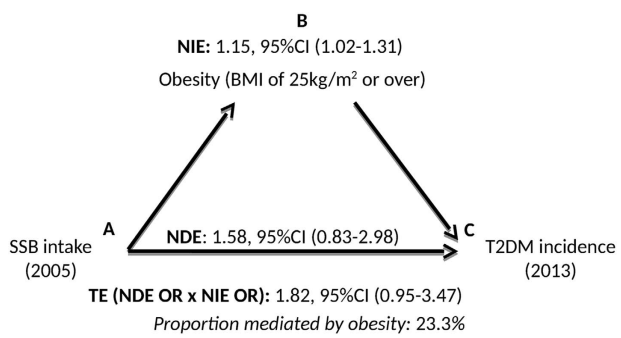

Figure 1. Mediation analysis investigating the association between SSB intake and T2DM incidence in 2013 mediated by obesity in 2009 in female TCS participants. Adjusted for baseline age, residence, education, income, leisure physical activity, smoking and drinking status, consumption of fruits and vegetables, consumption of deep fried food, and hypertension. NDE, natural direct effect; NIE, natural indirect effect; SSB, sugar-sweetened beverages; TE, total effect T2DM, type 2 diabetes mellitus.

Table 1. Baseline SSB consumption by sociodemographic and behavioural characteristics of eligible participants in the Thai Cohort Study[a]

Characteristics	*SSB consumption* N = *85 474*[a]			P-*value*[b]
	Rarely (N = *44 784*) n *(%)*[c]	*1–6 per week* (N = *34 113*) n *(%)*	⩾*1 a day* (n = *6577*) n *(%)*	
Men at risk in 2005	17 805 (46)	17 657 (46)	3013 (8.0)	< 0.001[d]
Median age (1st, 3rd quartile)	33 (27–40)	29 (25–35)	28 (24–34)	< 0.001[c]
Obese (⩾25.00 kg m^{-2})	4197 (24)	3616 (21)	621 (21)	< 0.001
>High school qualification	8179 (46)	7863 (45)	1183 (39)	< 0.001
Urban residence	8422 (48)	8918 (51)	1832 (61)	< 0.001
Income ⩾10,001 baht per month	7924 (46)	6527 (38)	1026 (35)	< 0.001
Regular/social drinkers	13 414 (76)	14 106 (81)	2261 (76)	< 0.001
Current smokers	3240 (19)	3857 (23)	788 (28)	< 0.001
⩾2 serves fruits/veg per day	16 425 (96)	16 533 (97)	2695 (95)	< 0.001
Deep-fried food eaten ⩾1 per day	1917 (11)	2870 (16)	1148 (38)	< 0.001
Physical activity (⩾8 per week)	11 073 (68)	11 452 (70)	1847 (67)	< 0.001
Women at risk in 2005	26 977 (57)	16 455 (35)	3564 (8.0)	< 0.001[d]
Median age (1st, 3rd quartile)	28 (24–35)	26 (23–31)	25 (22–30)	< 0.001[c]
Obese (⩾25.00 kg m^{-2})	2613 (10)	1582 (10)	382 (11)	0.108
>High school qualification	15 390 (57)	9325 (57)	1761 (50)	< 0.001
Urban residence	13 991 (52)	8601 (53)	2100 (59)	< 0.001
Income ⩾10,001 baht per month	8246 (31)	4143 (26)	814 (23)	< 0.001
Regular/social drinkers	13 268 (50)	9422 (58)	2069 (59)	< 0.001
Current smokers	212 (1.0)	171 (1.0)	83 (2.0)	< 0.001
⩾2 serves fruits/veg per day	25 696 (98)	15 557 (98)	3275 (97)	< 0.001
Deep-fried food eaten ⩾1 per day	3153 (12)	2754 (17)	1225 (34)	< 0.001
Physical activity (⩾8 per week)	12 643 (51)	7198 (47)	1486 (45)	< 0.001

Abbreviation: SSB, sugar-sweetened beverages. [a]Eligible participants at baseline did not have T2DM ($n = 902$) and were not missing SSB data ($n = 775$). Note for each tabulated characteristic the numbers vary a little due to missing data. [b]χ^2 comparing baseline characteristics among participants by SSB consumption. [c]number (%) in each category. For median age numbers in brackets are first and third quartiles and the final column records p-trend. [d]χ^2 comparing SSB consumption by sex.

Data access

Data are available through a data access agreement. All data access enquiries should be forwarded to Professor Adrian Sleigh and Associate Professor Sam-ang Seubsman (Principle investigators for the Thai Cohort Study).

Code availability

The programming code is available from KP.

RESULTS

Of the 87 151 initial TCS participants, 775 did not have valid SSB data and 902 reported diabetes at baseline so were excluded. Of the remainder, 39 175 were followed-up in 2013 of whom 695 reported a new diagnosis of diabetes.

The characteristics of all TCS participants by sex and baseline SSB consumption are shown in Table 1. Men consumed SSBs more frequently than women ($P < 0.001$). The median (first, third quartiles) age of participants who consumed SSBs more than daily at baseline was 28 (24, 34) among men and 25 (22, 30) among women; SSB consumption decreased with age in both sexes (*P*-trend < 0.001). Frequent SSB consumption was more prevalent among those who: lived in urban areas; had lower education levels; earned a lower income; smoked; drank alcohol regularly; frequently consumed deep-fried food; consumed < two serves of fruits and vegetables per day; or exercised ⩽daily (all $P < 0.001$). At baseline, men who rarely consumed SSBs were more likely to be obese ($P < 0.001$).

After adjusting for confounders (Table 2, model 2), baseline SSB intake was associated with an increased odds of T2DM in 2013 among women but not men. Among women, both moderate and high SSB intakes were associated with increased odds in 2013 (OR = 1.6, 95% CI 1.2–2.1 and OR = 2.4, 95% CI 1.5-3.9 respectively).

Table 2. Associations between SSB intake in 2005 and incidence of T2DM between 2005 and 2013 by sex

SSB intake at baseline in 2005	*Odds ratios (ORs) and 95% Confidence intervals (CI)*		
	Cases by 2013/at risk in 2005	*Model 1 OR (95% CI)*	*Model 2 OR (95% CI)*
Men			
Rarely	236/8860	1	1
1–6 times per wk	168/7516	1.1 (0.9–1.3)	1.0 (0.8–1.2)
⩾1 per day	33/1083	1.6 (1.1–2.3)	1.3 (0.9–2.1)
P trend		0.04	0.55
Women			
Rarely	142/13 291	1	1
1–6 times per wk	88/7133	1.5 (1.1–2.0)	1.6 (1.2–2.1)
⩾1 per day	28/1292	2.8 (1.8–4.2)	2.4 (1.5–3.9)
P trend		< 0.001	< 0.001

Abbreviations: BMI, body mass index; wk, week. Model 1: Age adjusted. Model 2: Adjusted for age, residence, education, income, physical activity, smoking and drinking status, consumption of fruits and vegetables, consumption of deep fried food, hypertension at baseline, and baseline BMI.

There was no evidence that the SSB-T2DM association was modified by age or BMI in either men or women.

We estimated that ~1% of T2DM in men and ~5% in women could be attributed to daily SSB consumption. Assuming a causal SSB intake-T2DM association, ~1500 T2DM cases in men and 2700 in women per year may have been prevented in the national Thai population if daily SSB consumption was avoided.

Mediation of incident T2DM in 2013 by obesity in 2009

Results from the logistic regression showed that amongst women, adjusting for BMI in 2009 slightly attenuated the associations between SSB consumption and development of T2DM in 2013 (unadjusted for BMI in 2009: OR = 1.6, 95% CI 1.1–2.3 and OR = 2.6, 95% CI 1.4–4.8 versus adjusted for BMI in 2009: OR = 1.5, 95% CI 1.0-2.3 (6% attenuation) and OR = 1.9, 95% CI 1.0–3.7 (27% attenuation), respectively; Supplementary Information).

In our counterfactual mediation analysis, the estimate for the natural indirect effect of SSB intake in 2005 on T2DM risk in 2013 was 1.15, 95% CI (1.02, 1.31), suggesting that 23% of the total association between 2005 SSB intake and T2DM risk in 2013 was mediated by obesity in 2009 (Figure 1).

Sensitivity analyses. Sensitivity analyses indicated that weight gain, waist circumference and waist-to-height ratio in 2009, as other measures of body fatness, were all mediators of the total effect of SSB intake in 2005 on T2DM risk in 2013 (Table 3). The proportions of the total effect of SSB intake on T2DM risk in 2013 mediated by these measures (2.9 to 32.9%) were similar to the proportion mediated by obesity. Using different cut-points of BMI gave mediated proportions ranging between 6.6 and 38.4%. Results in Table 3 show that for all of the investigated mediators, the proportion mediated by each of these measures increased as the cut off criteria for obesity increased.

The association between 2005 SSB consumption and risk of incident T2DM in 2009 was very similar to the association with risk of T2DM in 2013 (OR = 1.6, 95% CI 1.2–2.2 and OR = 2.2, 95% CI 1.3–3.6 respectively) among women suggesting that attrition between 2009 and 2013 is unlikely to have substantially influenced estimates.

DISCUSSION

In this prospective cohort of Thai adults we found that in women, SSB consumption was associated with increased odds of T2DM and this increased with more frequent consumption. We found that a moderate proportion of the SSB-T2DM relationship was mediated through BMI (23%) and that the proportion mediated increased with increasing BMI.

Potential limitations need to be considered when interpreting our findings. We had no information on consumption of non-carbonated sweetened beverages (that is, juices), nor did the questionnaire differentiate between sugar-sweetened and artificially sweetened beverages. The resultant misclassification is likely to have attenuated the relation between SSB intake and T2DM risk in this cohort (assuming a smaller association between artificially sweetened beverages and T2DM risk than SSBs). We also ascertained diabetes diagnoses through self-report, thus there will be some error in our classification of cases. However, a validation sub-study previously conducted amongst a sample of TCS participants indicated high accuracy of T2DM self-report, particularly among those who reported diabetes in both 2009 and 2013 (96%).[18] Thus, misclassification of diabetes status is unlikely to have materially altered our estimates.

There is an additional study consideration that should be emphasized. SSB consumption may be a possible marker of an overall unhealthy lifestyle. Therefore, although the casual logic linking SSB intake to diabetes risk is strong, it is possible that some of the effect in our study is due to unmeasured confounding by other factors associated with an unhealthy lifestyle. We had insufficient food frequency information to estimate the contribution of SSBs to total energy intake. However, other studies found that adjusting for energy did not negate the positive association between SSB intake and risk of T2DM.[29–31] Loss to follow-up was substantial with ~50% of the baseline cohort retained after eight years. For most variables, baseline distributions did not vary between participants who remained in the study and those not followed-up after 8 years. For some variables (regular SSB consumers, younger participants, and those underweight), rates of attrition were slightly higher. Given the evidence that these variables influence the risk of diabetes in this cohort, the higher attrition may have altered the SSB-T2DM effect estimation. However, the SSB-T2DM associations observed using only the 2009 incidence data (70% of baseline cohort) were similar suggesting such bias is likely to be minimal.

Our finding of an association between consumption of SSBs and increased risk of T2DM in women is consistent with findings from most studies in African,[10] Caucasian[10,11,32,33] and Asian populations.[12] One previous study found no association between SSB consumption and T2DM risk for men or women, although age differences may explain this; SSB consumption is more common in younger adults,[7] and the mean age of the Atherosclerosis Risk in

Table 3. Mediation analysis investigating the association between SSB intake and T2DM incidence in 2013 mediated by various measures of adiposity in 2009 in female TCS participants

Mediator in 2009	*Natural direct effect OR (95% CI)*	*Natural indirect effect OR (95% CI)*	*Total effect OR (95% CI)*	*Proportion mediated %*
Body mass index (BMI/m^2)				
BMI–overweight (23 kg m^{-2})	1.74 (0.93–3.26)	1.04 (0.95–1.15)	1.81 (0.96–3.42)	6.6
BMI–obese I (25 kg m^{-2})	1.58 (0.83–2.98)	1.15 (1.02–1.31)	1.82 (0.95–3.47)	23.3
BMI–obese II (30 kg m^{-2})	1.50 (0.77–2.93)	1.29 (1.04–1.61)	1.94 (0.98–3.84)	38.4
Weight gain (2005-2009)				
Gained 5 kg or more	1.95 (1.05–3.61)	1.02 (0.97–1.08)	1.99 (1.07–3.69)	2.9
Gained 10 kg or more	1.91 (1.03–3.56)	1.03 (0.96–1.11)	1.98 (1.06–3.67)	4.3
Waist Circumference				
80 centimetres or over	1.62 (0.82–3.21)	1.07 (0.98–1.18)	1.74 (0.88–3.46)	12.2
85 centimetres or over	1.43 (0.84–4.06)	1.19 (1.03–1.38)	1.71 (0.85–3.44)	32.4
Waist-to-height ratio				
0.5 or over	1.43 (0.70–2.93)	1.09 (0.97–1.21)	1.56 (0.76–3.20)	19.4
0.6 or over	1.34 (0.63–2.88)	1.16 (0.96–1.42)	1.57 (0.76–3.27)	32.9

Adjusted for baseline age, residence, education, income, leisure physical activity, smoking and drinking status, consumption of fruits and vegetables, consumption of deep fried food, and hypertension. *Proportion mediation = $\log(OR^{NIE})/\log(OR^{TE}) \times 100\%$ where NIE represents the natural indirect effect and TE represents the total effect.

Communities Study participants at baseline was 53.6[ref. 23] compared to 30.5 in our cohort.

A partial explanation for the sex specificity of the association may relate to energy requirements. Women generally have lower muscle mass than men hence lower metabolic energy needs[34] so similar SSB intake would contribute a larger proportion of total energy intake.[12] It may be that an association in men is only apparent at higher consumption levels than we observed here. Some studies found a relationship only in non-obese individuals.[10–12,32,33] We did not find effect-modification by obesity in this population. However, the prevalence of daily SSB consumption and obesity among these women was low and we may have lacked the statistical power to detect effect-modification by obesity in this cohort.

In keeping with previous studies, our results suggest that a moderate proportion of the SSB-T2DM relationship was mediated through BMI.[14,31,33] The proportion mediated through BMI increased with increasing obesity cutoffs, possibly reflecting the increasing T2DM risk with increasing BMI[22,35] or it may be that more obese participants were regularly drinking larger amounts of SSB. Most studies have investigated mediation by adjusting for BMI (the mediator) and assessing the change in the magnitude of the association. This approach can produce bias due to unmeasured mediator-outcome confounding or interaction between the exposure and mediator (SSB intake and BMI).[36] Here we assessed mediation using both a counter-factual mediation analysis and by adjusting for BMI in a standard regression model. Results were very similar using both approaches suggesting that unmeasured mediator-outcome confounding or interaction between the exposure and mediator are minimal for this association.

We had expected that a large proportion of the association between SSB intake and T2DM would be mediated by weight gain or obesity because SSBs can stimulate intake of other high glycaemic foods[37,38] leading to higher total caloric intake.[37,39,40] However, regular SSB consumption may increase T2DM risk through mechanisms independent of weight gain or obesity. For instance, high glycaemic loads from SSBs lead to repeated high insulin demand, which can contribute to compromised beta (β) cell function.[38] This may be particularly problematic in low and middle-income country Asian adults who may have experienced intrauterine or early childhood under-nutrition. This can lead to the under-development of β cell mass and an increased risk of T2DM later in life[41] independent of weight gain, especially with exposure to energy-dense foods like SSBs.[42,43]

CONCLUSION

The findings from this cohort suggest that at this point of the Thai health-risk transition SSB intake is increasing the risk of T2DM in women. As SSBs have no nutritional value and do not protect against disease they are an ideal target for public health efforts aimed at preventing increasing national T2DM incidence. Reducing the incidence and prevalence of T2DM in Thailand will require a multi-faceted approach. Targeting SSBs could serve as one focal point to prevent a national rise in the incidence of T2DM.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies this paper on the Nutrition & Diabetes website (http://www.nature.com/nutd)

Supplement 1: Associations between SSB intake in 2005 and incidence of T2DM in 2013 by sex

SSB intake at baseline in 2005	Cases in 2013/ At risk in 2005	Odds Ratios (ORs) and 95% Confidence Intervals (CI) Model 1 OR(95% CI)	Model 2 OR(95% CI)	Model 3 OR(95% CI)
Men				
Rarely	138/8,762	1	1	
1-6 times/wk	98/7,446	1.1(0.8-1.4)	1.0(0.7-1.3)	0.9(0.7-1.3)
≥1 per day	18/1,068	1.4(0.9-2.4)	1.0(0.6-1.9)	1.1(0.6-2.0)
P trend		0.24	0.95	0.85
Women				
Rarely	88/13,237	1	1	
1-6 times/wk	50/7,095	1.3(0.9-1.9)	1.6(1.1-2.3)	1.5(1.0-2.3)
≥1 per day	16/1,280	2.4(1.4-4.2)	2.6(1.4-4.8)	1.9(1.0-3.7)
P trend		<0.01	<0.01	0.01

Model 1-Age adjusted

Model 2-Adjusted for age, residence, education, income, physical activity, smoking and drinking status, consumption of fruits and vegetables, consumption of deep fried food, hypertension at baseline

Model 3-Adjusted for age, residence, education, income, physical activity, smoking and drinking status, consumption of fruits and vegetables, consumption of deep fried food, hypertension at baseline, and BMI in 2009

6

BODY MASS INDEX AND TYPE 2 DIABETES RISK: DEFINING THRESHOLDS AND POPULATION IMPACTS

6 BMI and T2DM risk: defining thresholds and population impacts

Chapter 6 is a peer-reviewed article that has been published in the *BMC Public Health*. It addresses Objective 4: to investigate the relationship between BMI and T2DM, and calculate population attributable risk. Longitudinal data from the 2005, 2009, and 2013 TCS surveys were used to reveal the sex-specific BMI thresholds associated with increased T2DM risk and to calculate the proportion of T2DM cases attributable to overweight and obesity in 2013. Participants were those who were diabetes free in 2005, had valid BMI data in 2005, and followed up over the eight-year period (N=39,021). Results demonstrated that a BMI cut-point of 22kg/m^2 could be justified for defining T2DM risk in Thai adults. As well, lowering obesity prevalence would greatly reduce T2DM incidence. These findings can help guide public health action and response.

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RESEARCH ARTICLE Open Access

Body mass index and type 2 diabetes in Thai adults: defining risk thresholds and population impacts

Keren Papier[1,2,5*], Catherine D'Este[1], Chris Bain[1,2], Cathy Banwell[1], Sam-ang Seubsman[3], Adrian Sleigh[1] and Susan Jordan[2,4]

Abstract

Background: Body mass index (BMI) cut-off values (≥25 and ≥30) that predict diabetes risk have been well validated in Caucasian populations but less so in Asian populations. We aimed to determine the BMI threshold associated with increased type 2 diabetes (T2DM) risk and to calculate the proportion of T2DM cases attributable to overweight and obesity in the Thai population.

Methods: Participants were those from the Thai Cohort Study who were diabetes-free in 2005 and were followed-up in 2009 and 2013 (n = 39,021). We used multivariable logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the BMI-T2DM association. We modelled non-linear associations using restricted cubic splines. We estimated population attributable fractions (PAF) and the number of T2DM incident cases attributed to overweight and obesity. We also calculated the impact of reducing the prevalence of overweight and obesity on T2DM incidence in the Thai population.

Results: Non-linear modelling indicated that the points of inflection where the BMI-T2DM association became statistically significant compared to a reference of 20.00 kg/m^2 were 21.60 (OR = 1.27, 95% CI 1.00–1.61) and 20.03 (OR = 1.02, 95% CI 1.02–1.03) for men and women, respectively. Approximately two-thirds of T2DM cases in Thai adults could be attributed to overweight and obesity. Annually, if prevalent obesity was 5% lower, ~13,000 cases of T2DM might be prevented in the Thai population.

Conclusions: A BMI cut-point of 22 kg/m^2, one point lower than the current 23 kg/m^2, would be justified for defining T2DM risk in Thai adults. Lowering obesity prevalence would greatly reduce T2DM incidence.

Keywords: Body mass index, Diabetes, Cut-points, Population attributable fraction, Asian cohort

Background

In recent decades, many low and middle-income countries (LMICs) have achieved substantial economic growth and this has led to increased urbanization, the adoption of new health behaviours (e.g. smoking and a 'western' diet), and an epidemiological shift from infectious diseases towards non-communicable diseases including type 2 diabetes mellitus (T2DM). These changes in health-risk behaviours, environment, and health outcomes, termed the 'health-risk transition', have been occurring in Thailand and T2DM now affects over four million adults [1].

Overweight and obesity significantly increase the risk of T2DM [2, 3] and their prevalence is increasing in Thailand [4]. Of concern, the association between body mass index (BMI) and T2DM risk is modified by ethnicity, with Asian populations having an increased risk of T2DM at BMI levels considered to be in the healthy weight range for Caucasian populations (<25 kg/m^2) [5]. Accordingly, in 2000 the World Health Organization (WHO) recommended that lower BMI cut-off points should be used to define overweight (23- < 25 kg/m^2)

* Correspondence: Keren.Papier@anu.edu.au
[1]National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, Australia
[2]Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane, Australia
Full list of author information is available at the end of the article

and obesity (≥25 kg/m^2) in Asian populations [6]. These recommendations were based on the few prevalence studies at the time [7–10]. In 2004, the WHO released an additional statement indicating that a range of BMI cut-off points may be necessary for guiding public health action in different Asian populations since the available data were inconsistent [11].

Since publication of these two recommendations, many studies assessed the validity of lower Asian-specific BMI cut-points for assessing diabetes, cardiovascular and mortality risk. Results were inconclusive, potentially due to confounders or exclusion of women [12], cross-sectional design [5, 13–15] or small samples of Asian participants [5, 16]. The prevalence of overweight and obesity are projected to continue to rise in Thailand. Understanding the optimal Southeast Asian BMI cut-off values associated with T2DM risk and the contribution of excess weight to the development of T2DM will have major implications for public health planning in Thailand. Therefore we examined the BMI threshold associated with T2DM risk in a large prospective cohort of adult Thais. We also estimated population attributable fractions and number of T2DM cases attributable to overweight and obesity in Thailand.

Methods

Study population

The Thai Cohort Study (TCS), is a nation-wide prospective investigation of the evolving 'health-risk transition' in Thailand [17]. TCS members (N = 87,151) were distance-learning students enrolled at Sukhothai Thammithirat Open University (STOU) who completed the baseline questionnaire in 2005 (44% of the total STOU student body). Follow-up questionnaires sent out in 2009 and 2013 were completed by 70% (n = 60,569) and 49% (n = 42,785) respectively of the original baseline cohort. The questionnaires collected information on a wide-range of topics including socio-demographic, health and lifestyle factors, and health outcomes (including diabetes).

Eligibility

Participants were eligible for this analysis if at baseline (2005) they reported not having diabetes and had a valid BMI (greater than 12.0), and provided a diabetes status in 2013.

T2DM Status

Participants were classified as having diabetes if they responded positively to the question "Have you ever received a confirmed diagnosis from a doctor that you definitely have diabetes?" by 2013. A validation study of self-reported diabetes among TCS participants, undertaken by a practicing Thai physician, indicated that the accuracy of diabetes self-report was high (82%), particularly among those who reported doctor-diagnosed diabetes in both 2009 and 2013 (96%) [18].

Body mass index

BMI was calculated using self-reported weight and height at baseline (Weight (kg)/ Height (meters^2)). A validation study indicated that these measures were accurate and reliable [19]. BMI was analysed as both a continuous and categorical variable. For the categorical variable, we created 8 categories (<18.5, 18.5 ≥ to <20.75, 20.75 ≥ to <23, 23 ≥ to <25, 25 ≥ to <27.5, 27.5 ≥ to <30, ≥ 30 to < 32.5, and ≥32.5) based on the 2000 International Task Force (ITF) [6] and the 2004 WHO [11] recommendations. To allow for finer grading of T2DM risk at lower BMI levels, we created two additional categories between 18.5 and 23.0 [5]. We combined the two highest categories into one because these groups were small.

Covariates

Potential confounders from the baseline questionnaire included socio-economic characteristics (income (≤10,000 Baht per month, 10,001–20,000 Baht per month, ≥20,001 Baht per month) and education level (Junior high school, High school, Diploma/Certificate, University)); demographic factors (age and childhood area of residence (urban/rural)); lifestyle factors (smoking (never smoked, ex-smoker, current smoker) and alcohol consumption (never, ex-drinker, occasional/social drinker, regular drinker)); fruit and vegetable consumption (categorised as < five or ≥ five serves/day), and consumption of sugar sweetened beverages (SSBs) (<3×/month, 1–6/week, 1 +/day). Leisure physical activity, reported as number of sessions per week of strenuous, moderate or mild exercise, was weighted ("2 × strenuous + moderate + mild + walking" exercise sessions) [20] and categorized by sessions per week (none, 1–7, 8–14, 15 or more) [21].

Statistical analysis

Since the relationship between diabetes and BMI may differ by sex, we conducted all analyses separately for men and women [22]. For eligible participants, baseline characteristics were compared for those with and without T2DM in 2013.

We used multivariable logistic regressions to assess the association between baseline BMI categories and development of T2DM by 2013. In Model 1 we estimated age-adjusted odds ratios (OR) and 95% confidence intervals (CI) for each BMI category (unadjusted for other variables). We then added potential confounders of the BMI-T2DM association (Model 2). These variables were identified using directed acyclic graphs (DAGs) based on theoretical knowledge and previous work with this cohort. They included age, area of residence during childhood, education, income, physical activity, consumption

of fruit/vegetables, sugar sweetened beverage intake [23], alcohol [24], and smoking [25].

We also modelled non-linear associations between baseline BMI (using a continuous term) and T2DM risk using restricted cubic splines with sex-specific distributions for BMI (using four knots, at 5th, 35th, 65th and 95th percentiles) [26]. To test for non-linearity, we compared one model with the linear BMI term to another model including the linear BMI term and its splined terms using a Wald test for men and women, respectively. We then determined the point of inflection as the lowest BMI value for which the association between BMI and T2DM was statistically significant using a BMI reference point of 20.00 and an increment of 0.01.

Since previous work with other Asian cohorts and Thai adults suggests that the relationship between BMI and T2DM risk could vary by age and urbanization status [11, 27] we stratified the models by baseline age (under 30, 30–39, and 40 or over) and childhood area of residence (rural versus urban). We also added the interaction terms of interest (categorical BMI x age or urbanization status x categorical BMI) to the main regression model (Model 3).

Proportion of T2DM cases attributable to overweight and obesity

We calculated population attributable fractions (PAFs) of overweight and obesity for each age-sex group using the standard formula [28] $PAF\% = \frac{\sum(px\times(OR-1)x)}{1+\sum(px\times(OR-1)x)} \times 100$

where px is the proportion of the population in the exposure level x (separate for overweight and obesity, categorized using the criteria of 23- < 25 kg/m^2 for overweight and ≥ 25 for obesity for comparability with previous studies) and OR-1 is the excess risk associated with exposure level x) to determine the proportion of T2DM in the cohort that could have been prevented if participants had a BMI of <23 kg/m^2. We then applied the sex-specific eight-year cumulative incidence and PAFs from this study to the total number of men and women in the national Thai population and divided the results by eight to estimate the annual number of T2DM cases in the national Thai population that could be attributed to a BMI of >23 kg/m^2 annually. As well, since we found the inflection points for BMI significantly associated with T2DM risk in TCS men and women were 21.60 and 20.03, we also calculated the effect of reducing BMI levels from <23 kg/m^2 to <22 kg/m^2 and from <23 kg/m^2 to <21 kg/m^2 in TCS men and women, respectively.

Impact of a theoretical 5% reduction in the prevalence of overweight and obesity in the TCS

We estimated the potential impact fraction (PIF) [29] that a 5% reduction in the prevalence of obesity and of overweight in the TCS cohort could have on T2DM incidence. This hypothetical impact was modelled as follows: 1) we reduced the prevalence of obesity (>25 kg/m^2) in the cohort to a level 5% below the original level and increased the prevalence of overweight (23- < 25 kg/m^2) by 5%; 2) we reduced the prevalence of overweight in the cohort by 5% and increased the prevalence of normal weight (<23 kg/m^2) by 5%. We calculated these PIFs using the formula [29] $PIF\% = \frac{((\sum p\times OR)-(\sum p^*\times OR))}{(\sum p\times OR)} \times 100$ *where p is the proportion of TCS members with overweight or obesity (categorized using the criteria of 23- < 25 kg/m^2 for overweight and ≥ 25 for obesity), OR is the odds of T2DM for each BMI category, and p* is an absolute 5% reduction in the real proportion of TCS members with overweight or obesity.*

Using the PIFs we calculated the hypothetical sex-specific T2DM incidence that would have occurred in the TCS had the prevalence of overweight and obesity been 5% lower. We then applied the observed and resulting hypothetical sex-specific T2DM incidences from our cohort to the national Thai population to estimate the number of T2DM cases that could be prevented annually if the hypothetical reductions in the prevalence of overweight and obesity were achieved.

All analyses were carried out using Stata (version 13.0). All statistical tests were two-sided.

Results

Of the 87,151 initial TCS participants, 60,569 were followed-up in 2009. Of these, 706 had prevalent diabetes in 2005 and 28 did not have a response for the diabetes question in 2009 and were excluded. Of the remaining 59,835, a total of 39,507 eligible participants (without missing diabetes responses) were followed-up in 2013. Of these, 486 did not have credible height or weight data. The final study sample included 39,021 participants of whom 688 reported a new diagnosis of diabetes (see flow chart in Additional file 1: Figure S1).

The baseline characteristics of participants by sex and diabetes status are shown in Table 1. Among both men and women, T2DM incidence increased with increasing age, BMI, and income ($p < 0.001$). T2DM incidence was double among those who lived in a city rather than a rural area as a child ($p < 0.001$). Among women, T2DM incidence was highest in those who consumed sugar-sweetened beverages (SSBs) daily ($p < 0.01$). Among men, T2DM incidence was highest in current smokers and those who consumed alcohol regularly ($p < 0.001$).

The age and multivariable adjusted sex-specific associations between baseline BMI and T2DM incidence by 2013 are shown in Table 2 and in Fig. 1. A BMI of 20.75- < 23.00 (compared to 18.5- < 20.75) was associated with higher T2DM risk in women (OR =3.0, 95% CI 1.6–5.7). In men, a

Table 1 Thai Cohort Study: baseline characteristics (2005) by diabetes outcome in 2013

	Men $N = 17607$[a]			Women $N = 21900$[a]		
	T2DM incidence[c]	%[d]	p [e]	T2DM incidence [c]	%[d]	p [e]
Total	438/17607	2.5		260/21900	1.2	
Age years						
Under 30	61/7029	0.9	<0.001	60/12097	1.0	<0.001
30–39	166/6634	2.5		108/7101	1.5	
40 or over	211/3944	5.4		92/2702	3.4	
BMI-Asian (kg/m^2) cut-points[b]						
Underweight (≤18.49)	5/962	0.5	<0.001	3/4221	0.1	<0.001
Normal (18.5- < 23.0)	67/8208	0.8		56/12789	0.4	
At risk (23.0- < 25.0)	76/4034	1.9		45/ 2347	1.9	
Obese I (25.0- < 30.0)	196/3631	5.4		98/ 1858	5.3	
Obese II (≥30.0)	86/520	16.5		56/ 451	12.4	
Income (Baht/month)						
≤ 10,000	146/ 8930	1.6	<0.001	121/ 13,996	0.9	<0.001
10,001–20,000	148/ 5590	2.7		79/ 5338	1.5	
≥ 20,001	134/ 2820	4.8		54/ 2087	2.6	
Education level						
Junior high school	21/ 769	2.7	0.16	6/ 376	1.6	0.90
High school	177/ 7991	2.2		94/ 7948	1.2	
Diploma/certificate	101/ 3994	2.5		79/ 6670	1.2	
University	137/ 4815	2.8		79/ 6849	1.2	
Childhood area of residence						
Rural	290/13377	2.2	<0.001	158/ 15,871	1.0	<0.001
Urban	141/ 4045	3.5		96/ 5846	1.6	
Fruit and vegetable serves/day						
< 5 serves	310/ 11,658	2.7	0.05	156/ 12,619	1.2	0.37
≥ 5 serves	115/ 5360	2.2		95/ 8625	1.1	
Sugar sweetened beverage intake						
Less than daily	404/ 16,376	2.5	0.24	230/ 20,424	1.1	<0.01
≥ daily	33/ 1083	3.0		28/ 1292	2.2	
Smoking						
Never smoked	147/ 8342	1.8	<0.001	237/ 20,290	1.2	0.17
Ex-smoker	151/ 5437	2.8		6/ 691	0.9	
Current smoker	115/ 3024	3.8		4/ 149	2.7	
Alcohol intake						
Never drinks	29/ 1868	1.6	<0.001	123/ 9005	1.4	0.14
Quit	59/ 1777	3.3		12/ 1475	0.8	
Occasional drinker	280/ 12,037	2.3		119/ 11,012	1.1	
Regular drinker	67/ 1780	3.8		1/ 120	0.8	

[a]Numbers may not add to total sample size due to missing responses for some characteristics
[b]Body mass Index (BMI) defined using the WHO International Obesity Taskforce recommendations
[c]Incident cases cumulating by 2013 divided by population without diabetes at baseline
[d]Cumulative incidence over 8 years T2DM, type 2 diabetes mellitus
[e]Chi Square *p* value comparing baseline characteristics among participants by T2DM status in 2013

Table 2 Association between baseline body mass index and eight-year incidence of type 2 diabetes

Body Mass Index (kg/m^2) at baseline in 2005	Incident cases by 2013[a]	Adjusted OR estimates relating BMI and T2DM	
		Model 1[b] OR (95% CI)	Model 2[c] OR (95% CI)
Men			
< 18.5	5/968	0.94 (0.34–2.5)	0.85 (0.28–2.6)
18.5 - <20.75	19/3232	1	1
20.75 - <23.0	48/4970	1.4 (0.80–2.3)	1.2 (0.69–2.2)
23.00 - < 25.00	77/ 4054	2.3 (1.4–3.8)	2.3 (1.3–3.9)
25.00 - <27.50	120/ 2583	5.5 (3.4–9.0)	5.5 (3.2–9.2)
27.50 - <30.00	75/1028	8.6 (5.1–14.4)	8.1 (4.7–14.1)
30.00 - <32.50	52/369	20.2 (11.7–34.8)	22.6 (12.7–40.1)
32.5 and over	34/151	42.3 (23.3–77.1)	43.3 (22.9–81.6)
Women			
< 18.5	3/4222	0.35 (0.10–1.2)	0.44 (0.12–1.5)
18.5 - <20.75	18/7602	1	1
20.75 - <23.0	38/5186	2.7 (1.5–4.7)	3.0 (1.6–5.7)
23.00 - <25.00	45/2373	6.1 (3.5–10.6)	6.7 (3.6–12.4)
25.00 - <27.50	63/1292	16.4 (9.6–27.9)	14.9 (8.1–27.5)
27.50 - <30.00	35/543	21.6 (12.0–38.7)	23.0 (12.0–44.1)
30.00 - <32.50	23/265	31.1 (16.4–58.8)	34.9 (17.4–69.7)
32.5 and over	33/183	78.6 (43.1–143.4)	73.5 (37.0–146.2)

ORs Odds ratios, *CI* Confidence Interval, *BMI* Body Mass Index in kg/m^2 T2DM, type 2 diabetes mellitus
[a]Incident cases cumulating by 2013 divided by population without diabetes at baseline
[b]Model 1 is age adjusted
[c]Model 2 is adjusted for age, education, income, area of childhood residence, physical activity, smoking, alcohol intake, fruit and vegetable intake, and sugar sweetened beverage intake. These variables were selected using directed acyclic graphs (see methods)

BMI of 23 < 25 (compared to 18.5- < 20.75) was associated with higher T2DM risk (OR = 2.3, 95% CI 1.3–3.9). The cubic spline non-linear modelling of BMI's effect on T2DM showed that the points of inflection where the association became statistically significant compared to a reference of 20.00 kg/m^2 for men and women were 21.60 (OR = 1.27, 95% CI 1.00–1.61) and 20.03 (OR = 1.02, 95% CI 1.02–1.03), respectively. In women, BMI levels <20 kg/m^2 appeared to be inversely associated with risk suggesting thresholds might be even lower for women, however, few participants fell into these categories thus definite conclusions are difficult to draw. At a BMI of 25.0 kg/m^2, T2DM risk was exponentially increased in both men (OR = 4.3, 95% CI 3.0–6.1) and women (OR = 11.6, 95% CI 6.8–19.8.),

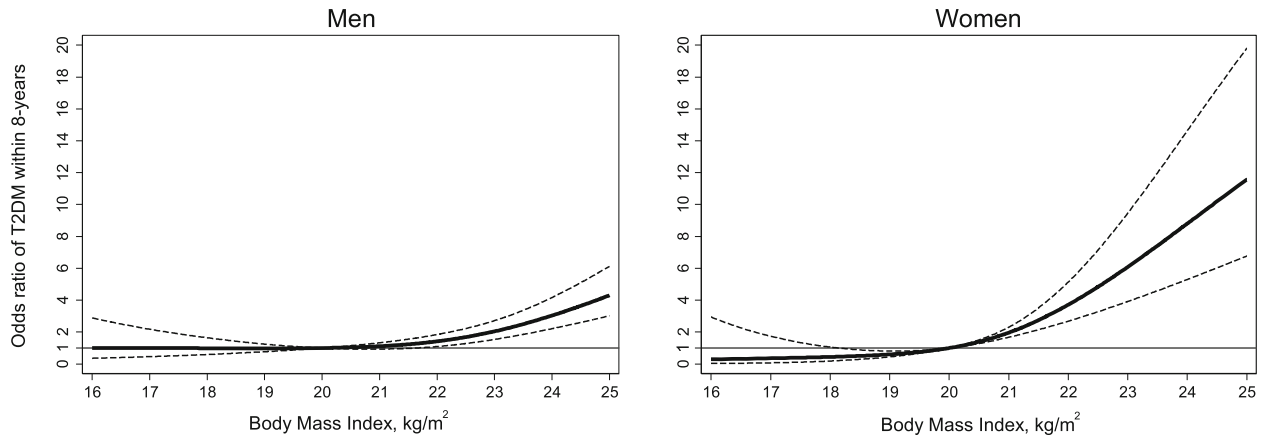

Fig. 1 Odds ratios of type 2 diabetes incidence (2005–2013) according to body mass index in 2005. - - - - 95% Confidence Interval T2DM risk modelled using restricted cubic splines with knots at 5th, 35th, 65th and 95th. Body mass index reference was set at 20.00 kg/m^2

respectively. These findings suggest that the exponential relationship between BMI and T2DM is greater among women than men and that excess adiposity in Southeast Asian women has major implications for T2DM risk even at BMI levels considered to be in the healthy weight range for Asian populations (<23 kg/m^2) (Fig. 1).

Figure 2 shows the sex-specific association between baseline BMI and eight-year T2DM incidence stratified by age and urbanization status. Among men, while the association between obesity (BMI ≥ 25) and risk of T2DM was higher among participants aged ≤30 (OR = 15.7, 95% CI 7.9–31.4) than those aged 40 and older (OR = 4.60, 95% CI 2.98–7.11) the interaction term between BMI and age was not statistically significant (p = 0.47). Among women, there was some indication that the BMI-T2DM association was modified by area of residence as a child such that the association between high BMI categories (≥ 23 and ≥25) and T2DM risk was higher in participants who lived in an urban area of residence as a child (BMI ≥ 23: OR = 6.8, 95% CI 3.1–15.0; ≥ 25 OR = 24.6, 95% CI 12.7–47.7) than those who lived in a rural area of residence as a child BMI ≥ 23: OR = 3.3, 95% 1.9–5.5; BMI ≥ 25: OR = 10.8, 95% 7.1–16.3), however, the interaction term between BMI and urbanization status was not statistically significant at the 5% level (p = 0.08).

Proportion of T2DM cases attributable to overweight and obesity

We estimated that around 63% of T2DM in men and 62% in women could be attributed to overweight or obesity

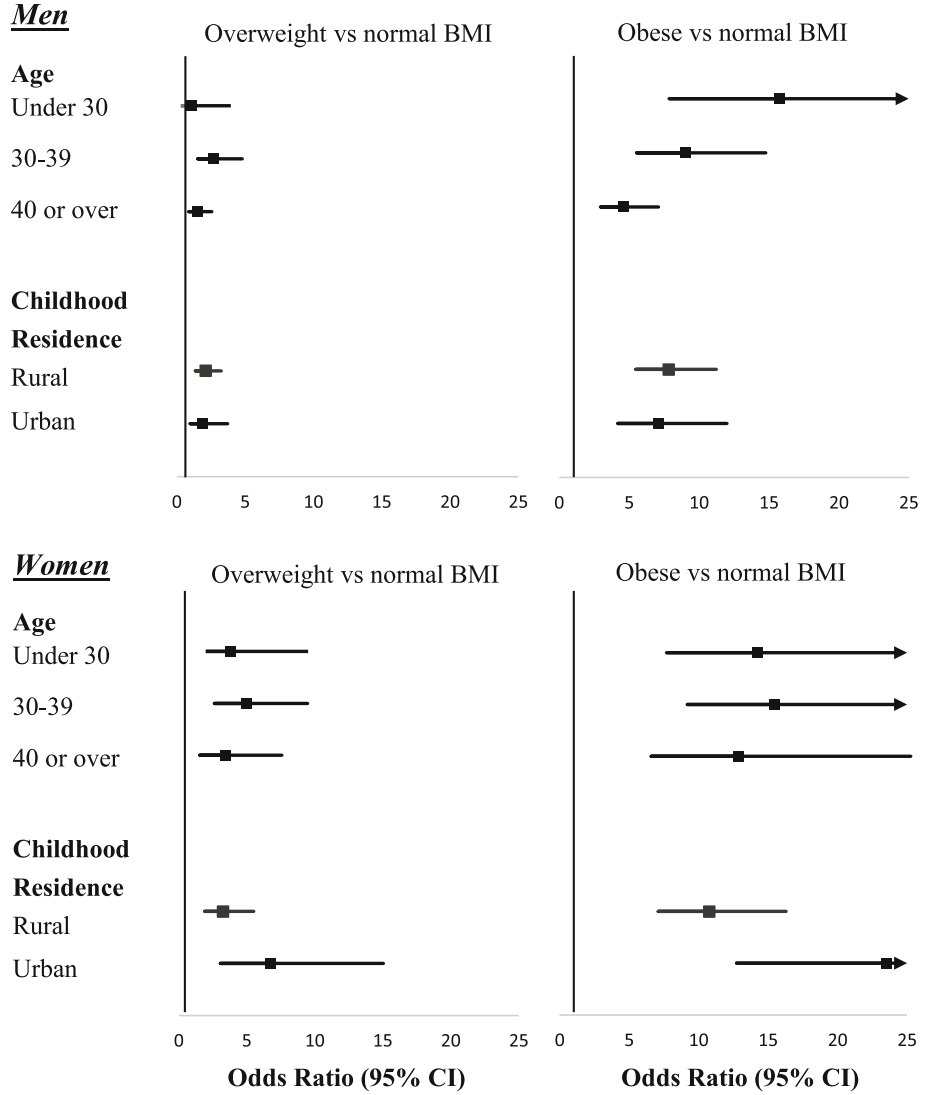

Fig. 2 Odds ratios of type 2 diabetes by body mass index stratified by age and residence CI confidence interval Overweight: Body Mass Index (BMI) 23.00 - < =24.99 kg/m^2 and Obesity BMI ≥25.00 kg/m^2 Adjusted for age, education, income, area of childhood residence, physical activity, smoking, alcohol intake, fruit and vegetable intake, and sugar sweetened beverage intake

(Table 3). Assuming the association between BMI and T2DM is causal, an estimated 66,000 cases in men and 32,000 in women per year may have been prevented in the national Thai population if a BMI level of <23 kg/m^2 was maintained across the population. Moreover, reducing BMI levels from <23 kg/m^2 to <22 kg/m^2 and from <23 kg/m^2 to <21 kg/m^2 in TCS men and women, respectively would have prevented a further 6700 cases in men and 9500 cases in women annually, in the national Thai population.

Potential impact of reducing the prevalence of overweight and obesity in the TCS

Our results suggest that if the prevalence of overweight could be reduced by 5% then this could result in a slight reduction in T2DM cases annually in the national Thai population (male PIF 2.0%, cases prevented per year = 1300; female PIF 6.0%, cases prevented per year = 1900). A 5% reduction in the prevalence of obesity would have a more profound effect, potentially preventing ~6600 cases in men (PIF 10%) and ~6100 in women (PIF 19%) in the national Thai population.

Discussion

Our prospective nationwide study of Thai adults provides further evidence that T2DM risk is increased at BMI levels below 25 kg/m^2 in Asian populations and that the use of lower Asia-specific BMI cut-points are necessary for defining T2DM risk in Asian adults, particularly in women. We found that T2DM risk was associated with a BMI of 22 kg/m^2 and 20 kg/m^2 in men and women, respectively. We also found that for the same BMI level the association between BMI and T2DM risk was higher in women and that their T2DM risk was already increased at BMI levels currently considered in the 'healthy range' for Caucasian and Asian populations. Over 60% of all T2DM cases occurring in this cohort could be attributed to overweight and obesity and our results suggest that a hypothetical 5% reduction in the prevalence of obesity could result in almost 13,000 fewer cases of T2DM annually in the national Thai population.

There are several potential limitations which should be considered when interpreting our findings. All data on height, weight and diabetes diagnoses were ascertained using self-report. Accordingly, there may be some misclassification error which should be considered when interpreting these findings. However, validation studies of self-reported diabetes [18] and self-reported weight and height [30] in this cohort have shown that the accuracy of these self-reported measures is high. Another potential issue is attrition. Over the eight-year follow-up, 50% of the baseline cohort was lost to follow-up. Slight differential attrition was noted by body size with a higher retention rate for participants with a larger weight at baseline. However, previous work with this cohort showed that ORs for the association between BMI and T2DM incidence in the first 4 years (70% retention of baseline cohort) were similar to those from the total eight-year follow-up, indicating that eight-year ORs are likely to be generalizable [21]. Moreover, non-differential attrition was noted by sex, dietary intake, alcohol intake, and area of residence indicating that these variables would unlikely affect BMI-T2DM risk effect estimates (see Additional file 2: Table S1).

An additional issue to consider is the precision of the PAF and PIF estimates. These measures are dependent on the accuracy and the magnitude of the ORs and the prevalence estimates being used. Accordingly, there is potential for error in these estimates due to variations in the accuracy in the self-report of weight and height, differences in the prevalence of overweight and obesity between our cohort and the national Thai population, as well as any risk estimates affected by attrition in this cohort. There is no agreed method for calculating confidence intervals on composite measures such as PAF and PIF estimates. Accordingly, these were not calculated. Nevertheless, our PIF and PAF estimates highlight the potential magnitude of the effects of overweight and obesity on T2DM incidence in Thai adults.

Important strengths of this study include the large sample of Thai adults and our nationwide coverage. Moreover, to our knowledge this is the largest prospective study to assess the BMI cut-points associated with T2DM risk and the number of T2DM cases attributed to overweight and obesity in adults living in Southeast Asia.

This study found that T2DM risk is increased at BMI levels considered to be in the 'normal' range for Caucasian populations (<25 kg/m^2). Our findings are consistent with previous studies that recommend using a BMI cut-off between 21 and 24 kg/m^2 to define overweight and obesity in Asian populations based on diabetes and cardiovascular risk [5, 13–15, 31–33]. However, studies of body size and mortality could shed light on appropriate cut-offs for BMI on health more generally. For example, a few mortality studies conducted in different Asian populations did not find evidence that mortality risk was increased at BMI levels <25 kg/m^2 [34]. However, these studies were unable to adjust for potential confounding effects of factors such as infectious diseases and the prevalence of smoking in these different populations. Adjusting for related factors in this study had minimal influence on the BMI-T2DM relationship. However, these factors might modulate more of the BMI-mortality association than the BMI-T2DM relationship [35].

A likely explanation for the increased risk of T2DM at these low levels of BMI is body composition. Evidence suggests that the relationship between BMI and body fat differs by ethnicity, with Asian populations having higher proportions of body fat compared to muscle mass

Table 3 Thai Cohort Study: population attributable fraction[d] of diabetes due to excess weight

	Overweight			Obese			Total[b]
Age group	Percent[a]	Odds Ratio[c] (95% CI)	PAF%	Percent[a]	Odds Ratio[c] (95% CI)	PAF%	PAF %
Men							
< 30	16.0	1.10 (0.30–3.96)	0.5	13.9	15.73 (7.87–31.4)	66.8	67.3
30–39	26.8	2.72 (1.54–4.80)	12.5	27.5	9.06 (5.55–14.78)	60.3	72.8
≥ 40	28.2	1.51 (0.89–2.56)	5.8	36.9	4.60 (2.98–7.11)	53.8	59.6
Total	21.6	2.06 (1.44–2.96)	8.5	22.2	7.65 (5.69–10.28)	54.6	63.1
Women							
< 30	6.6	3.78 (1.50–9.52)	8.8	6.8	14.24 (7.70–26.3)	43.0	51.8
30–39	13.0	4.98 (2.62–9.48)	15.0	13.3	15.50 (9.19–26.2)	56.0	71.0
≥ 40	21.8	3.44 (1.56–7.58)	12.6	22.5	12.91 (6.59–25.27)	63.6	76.2
Total	9.8	4.13 (2.68–6.35)	11.6	9.8	14.23 (10.11–20.02)	50.0	61.6

CI confidence interval, *PAF* Population Attributable Fraction
Overweight: Body Mass Index (BMI) 23.00- < =24.99 kg/m^2 and Obesity: BMI ≥25.00 kg/m^2
[a]Prevalence
[b]Overweight and Obesity combined
[c]Odds ratios (ORs) associating baseline body mass index and eight-year incidence of type 2 diabetes between 2005 and 2013. All ORs are adjusted for age, education, income, area of childhood residence, physical activity, smoking, alcohol intake, fruit and vegetable intake, and sugar sweetened beverage intake
[d] PAF% calculated using the formula $PAF\% = \frac{\sum (px \times (OR-1)x)}{1+\sum (px \times (OR-1)x)} \times 100$

than Caucasian populations when matched by age and BMI [36]. Ethnicity related differences in body fat composition and distribution may be associated with epigenetic programming [37]. Babies that develop in an undernourished intrauterine environment have been shown to experience 'catch up' growth later in life that has been associated with preservation of adipose tissue, obesity, and increased insulin resistance [38]. As well, children growing up with under-nutrition and frequent infection who survive to adulthood have low attained height, and a life-long threat of adult obesity, which is widespread in Thailand today [39]. Many Asian populations have experienced generations of under-nutrition prior to experiencing the accelerated nutrition transition currently underway in much of Asia. Accordingly, some Asian populations may be more predisposed to storing visceral fat or are more insulin resistant at lower levels of adiposity [36, 40].

Effects of epigenetic programming may be particularly intensified when there is a strong mismatch between the intrauterine and early life environments [41], which may explain the potentially increased association between obesity and T2DM incidence noted in TCS females who lived in an urban area of residence during childhood. Living in an urban area during childhood has been shown to be associated with increased exposure to an energy-dense western diet, reduced physical activity and a higher prevalence of obesity during adulthood [42]. Therefore, unlike children who are raised in a rural area of residence and may have low exposure to the 'western diet', those who are raised in an urban area of residence may have pro-longed exposure to an obesogenic environment and consequently an increased risk of T2DM later in life.

As in previous studies, this study found that for the same BMI T2DM risk was higher in women [22]. Evidence suggests that this sex-specific association may be related to differences in body composition and hormones between men and women. For instance, men have higher concentrations of testosterone than women and testosterone has been shown to inversely associate with adiposity and insulin resistance in men [43]. This effect may relate to testosterone's role in increasing lean body mass and decreasing inflammatory cytokines, which can increase insulin resistance [43]. These findings highlight the need for public health interventions to target the promotion of healthy weight differently in Asian men and women.

Our findings show that the public health impact of preventing or reducing the prevalence of obesity in Thailand could be profound. Shifting as little as 5% of the population with obesity to a lower BMI of 23- < 25 kg/m^2 could lead to a substantial decrease in the number of T2DM cases occurring in the Thai population; and this benefit could be even greater than we have calculated considering the high and increasing prevalence of obesity, particularly in women, in the national Thai population [27].

Conclusions

The findings from this prospective study of Thai adults suggest that using lower BMI cut-points is necessary for defining T2DM risk in Southeast Asian populations. Our findings suggest that T2DM risk is already increased at BMI levels <23 kg/m^2. Therefore, public health action and response may be required at lower BMI levels to help curb the T2DM epidemic currently

underway in Southeast Asia. Further research is required to confirm these findings in different Southeast Asian populations.

Additional files

Additional file 1: Figure S1. Selection of the analysed cohort from the Thai Cohort Study. (PDF 345 kb)

Additional file 2: Table S1. Baseline characteristics for participants versus non-participants. (DOCX 14 kb)

Abbreviations

BMI: Body mass index; CI: Confidence intervals; DAG: Directed acyclic graph; ITF: International Task Force; LMICs: Low and middle-income countries; OR: Odds ratios; PAF: Population attributable fraction; PIF: Potential impact fraction; SSBs: Sugar sweetened beverages; STOU: Sukhothai Thammithirat Open University; T2DM: Type 2 diabetes mellitus; WHO: World Health Organization

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Availability of data and materials

The datasets used during the current study are available from the principle investigators of the Thai Cohort Study (Professor Adrian Sleigh and Associate Professor Sam-ang Seubsman) on reasonable request.

Authors' contributions

KP devised the study, analysed all of the data and wrote the paper. SJ assisted with the planning of the study, guided the analytical approach of this paper, and helped with the interpretation of the findings. CD'E guided the analytical approach of this paper, supervised all analyses of the data and helped with the interpretation of the study findings. CBain, CBanwell, AS and SS assisted with the interpretation of the findings and with the editing of all drafts. AS and SS conceived and developed the cohort. All authors approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for the study was obtained from STOU Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocols 2004/344, 2009/570). All participants gave informed written consent and data were de-identified before analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Author details

[1]National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, College of Medicine, Biology and Environment, The Australian National University, Canberra, Australia. [2]Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane, Australia. [3]Thai Health-Risk Transition Study, School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi, Thailand. [4]The School of Public Health, The University of Queensland, Brisbane, Australia. [5]National Centre for Epidemiology & Population Health, The Australian National University, Building 62, Mills Road, Canberra, ACT 2601, Australia.

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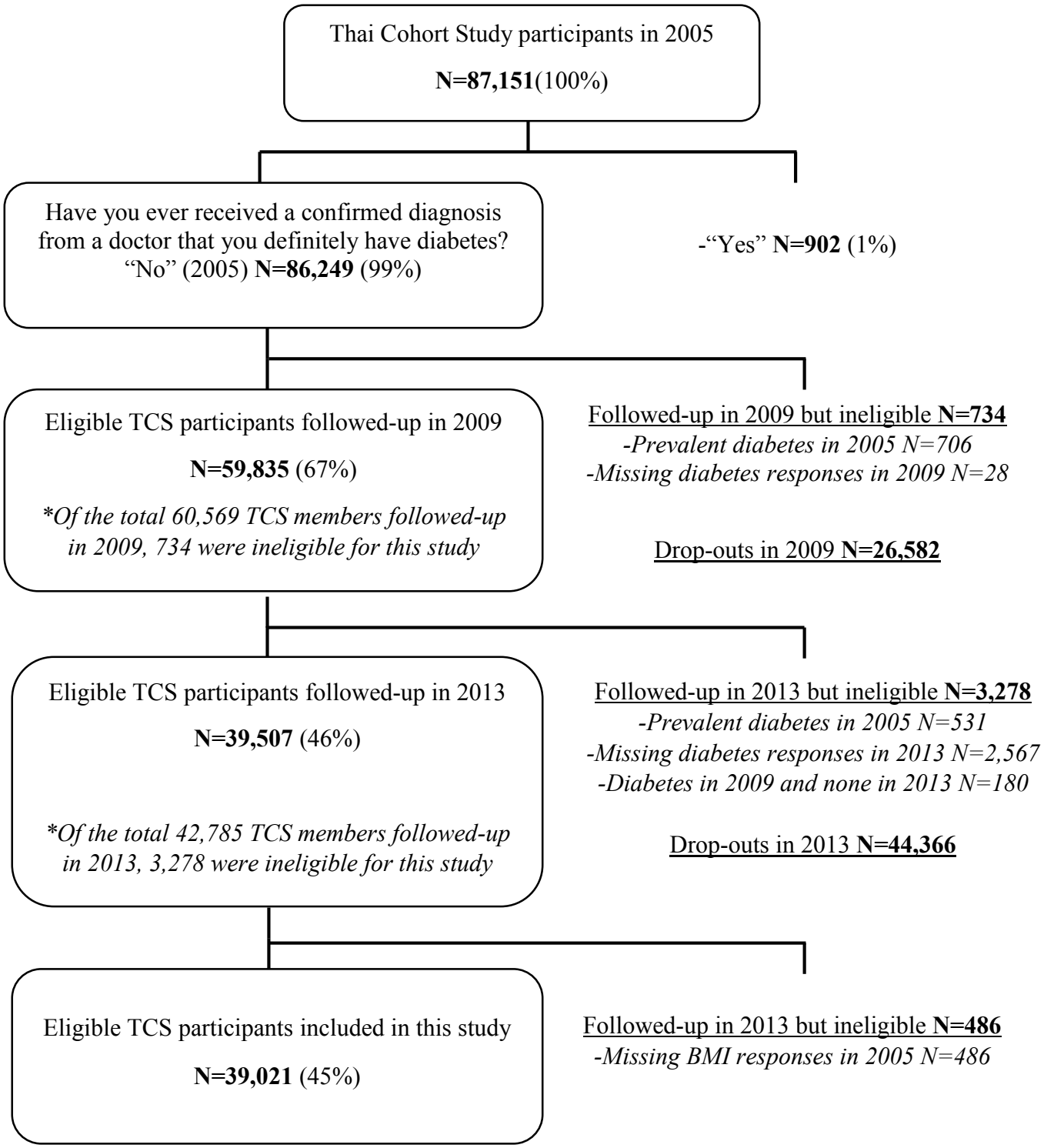
Supplement 1: Selection of the analysed cohort from the Thai Cohort Study



Supplement 2: Baseline characteristics for participants *versus* non-participants

Baseline characteristics	Non participants* n (%)	Study participants* n (%)	P value**
Total	48,130 (55%)	39,021 (45%)	
Sex			<0.001
Men	22,129(46)	17,355(44)	
Women	25,994(54)	21,666(56)	
Age years			<0.001
Under 30	31,304(65)	18,963(48)	
30-39	11,951(25)	13,570(35)	
40 or over	4,857(10)	6,488(17)	
BMI-Asian cut-points†			<0.001
Underweight (≤18.49	7,475(16)	5,183(13)	
Normal (18.5-22.9)	25,817(55)	20,997(54)	
At risk (23.0-24.9)	6,588(14)	6,381(16)	
Obese I (25.00-29.9)	5,830(12)	5,489(14)	
Obese II (≥30.0)	1,270(3)	971(3)	
Residence			<0.001
Rural	22,423(47)	19,326(50)	
Urban	25,295(53)	19,469(50)	
Education			<0.001
Junior high school	1,920(4)	1,119(3)	
High school	23,728(49)	15,687(40)	
Diploma/certificate	12,890(27)	10,578(27)	
University	9,439(20)	11,547(30)	
Income (Baht/month)			<0.001
≤10,000	32,794(70)	22,641(59)	
10,001-20,000	9,759(21)	10,811(28)	
≥20,001	4,116(9)	4,840(13)	
Smoking			<0.001
Never smoked	32,812(72)	28,313(76)	
Ex-smoker	7,373(16)	6,036(16)	
Current smoker	5,410(12)	3,129(8)	
Alcohol intake			<0.001
Never	11,984(25)	10,728(28)	
Used to drink (quit)	4,519(10)	3,205(8)	
Occasional/Social	28,587(60)	22,785(59)	
Regular drinker	2,289(5)	1,882(5)	

*Numbers may not add to total sample size due to missing responses for some characteristics

**$\chi 2$ comparing each baseline characteristic by participation status

† Body mass Index (BMI) in kg/m^2, categorized by Asian cut-offs using the WHO International Obesity Taskforce recommendations

7

SOCIAL DEMOGRAPHY OF TRANSITIONAL DIETARY PATTERNS IN THAI ADULTS

7 Social demography of dietary patterns in Thai adults

Chapter 7 is a peer-reviewed article that has been published in *Nutrients*. It addresses Objective 5: to determine the association between upstream T2DM risk factors and dietary patterns. A dietary survey was conducted with a random sample of TCS participants who were followed-up in 2013 to assess dietary patterns in 2015 (N=1,075). Results reported here demonstrate four transitional dietary patterns and their socio-demographic predictors. These findings highlight the groups who are most at risk of consuming an unhealthy diet. This information is useful for T2DM control efforts in Thailand and could support efforts to nudge the population towards healthier choices.

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Article

Social Demography of Transitional Dietary Patterns in Thailand: Prospective Evidence from the Thai Cohort Study

Keren Papier [1,2,*], Susan Jordan [2,3], Catherine D'Este [1,4], Cathy Banwell [1], Vasoontara Yiengprugsawan [1,5], Sam-ang Seubsman [6] and Adrian Sleigh [1]

1 National Centre for Epidemiology and Population Health (NCEPH) and Department of Global Health, Research School of Population Health, ANU College of Health & Medicine, The Australian National University, Canberra 2601, Australia; Catherine.Deste@anu.edu.au (C.D.); Cathy.Banwell@anu.edu.au (C.B.); vasoontara.yieng@anu.edu.au (V.Y.); Adrian.Sleigh@anu.edu.au (A.S.)
2 Population Health Department, QIMR Berghofer Medical Research Institute, Brisbane 4006, Australia; Susan.Jordan@qimrberghofer.edu.au
3 The School of Public Health, The University of Queensland, Brisbane 4006, Australia
4 School of Medicine and Public Health, Faculty of Health and Medicine, The University of Newcastle, Newcastle 2308, Australia
5 Centre for Research on Ageing, Health and Wellbeing, Research School of Population Health, The Australian National University, Canberra 2601, Australia
6 Thai Health-Risk Transition Study, School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi 11120, Thailand; sam-ang.seu@stou.ac.th
* Correspondence: Keren.Papier@anu.edu.au; Tel.: +61-73845-3502

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Abstract: In recent decades, a health-risk transition with changes in diet and lifestyle in low and middle-income countries (LMICs) led to an emergence of chronic diseases. These trends in Southeast Asian LMICs are not well studied. Here, we report on transitional dietary patterns and their socio-demographic predictors in Thai adults. Dietary data in 2015 were from a random sub-sample (N = 1075) of 42,785 Thai Cohort Study (TCS) members who completed all three TCS surveys (2005, 2009, 2013). Principle Component Analysis identified dietary patterns and multivariable linear regression assessed associations (Beta estimates (ß) and confidence intervals (CIs)) between socio-demographic factors and dietary intake pattern scores. Four dietary patterns emerged: Healthy Transitional, Fatty Western, Highly Processed, and Traditional. In women, higher income (≥30,001 Baht/month vs. ≤10,000) and managerial work (vs. office assistant) was associated with lower scores for Traditional (ß = −0.67, 95% CI −1.15, −0.19) and Fatty Western diets (ß = −0.60, 95% CI −1.14, −0.05), respectively. University education associated with lower Highly Processed (ß = −0.57, 95% CI −0.98, −0.17) and higher Traditional diet scores (ß = 0.42, 95% CI 0.03, 0.81). In men and women, urban residence associated with higher Fatty Western and lower Traditional diets. Local policy makers should promote healthy diets, particularly in urban residents, in men, and in low-SEP adults.

Keywords: socioeconomic status; diet patterns; Asian cohort; urban; nutrition transition; principle component analysis

1. Introduction

Rapid economic growth in low and middle-income countries (LMICs) has resulted in transformation of food systems and diets with a remarkable increase in the intake of animal fats and sugars. Concurrent urbanization and decreased physical activity is leading to increased body size

and an epidemic of unfamiliar non-communicable diseases (NCDs), including diabetes, hypertension, and ischemic heart disease [1].

Collectively, these shifts in environment, behaviour, and disease, together with the health system response, have been termed the "health-risk transition" [2]. The nutritional components of the health-risk transition have been long recognized as a "nutrition transition" [3]. The changes in lifestyle behaviours and disease outcomes generally occur first in urban residents who have a high socio-economic position (SEP) [4]. Indeed, some studies from developing LMICs have found that urban, high SEP individuals have a higher prevalence of NCDs and are more likely to consume diets that are associated with an increased NCD risk than rural, low-SEP individuals [5,6]. However, recent evidence suggests that as more economic development occurs, the transition deepens and unhealthy diets and the NCDs shift to rural and low SEP individuals [6–11] This pattern resembles what is commonly observed in high income countries (HICs) that are at the advanced stage of the health-risk transition [12,13].

Thailand is a LMIC that has achieved substantial economic growth in recent decades [14] and now has an emerging type 2 diabetes (T2DM) epidemic [15]. The socio-demographic determinants of dietary intake in Southeast Asian countries like Thailand are not well understood. A few small, cross-sectional studies suggest that social differences in diet and health outcomes among Thai adults are beginning to resemble what is commonly observed in countries at the later stages of the nutrition transition (e.g., higher prevalence of obesity in rural and low SEP women; higher consumption of healthy foods in wealthy men and women) [16,17]. However, it is unclear how socio-demographic factors associate with dietary patterns in Thai adults. Understanding the drivers of dietary patterns will allow for the development of more targeted public health interventions that are aimed at controlling the T2DM epidemic. In this study, we identify major dietary patterns and examine the associations between socio-demographic factors and dietary patterns in a cohort of Thai adults.

2. Materials and Methods

Members of the Thai Cohort Study (TCS) were the source population for this research. The cohort is a prospective study of the "health-risk transition" among Sukhothai Thammathirat Open University (STOU) students that are residing nationwide [18]. In 2005, all 200,000 enrolled students were invited to participate and were mailed a questionnaire covering a wide array of variables including socio-demographic, health and lifestyle factors, and health outcomes. These were distance learning students, mostly part time and a little more urbanized than the national population, using education for self-improvement. As such, they are likely to experience the "health-risk transition" ahead of their fellow Thais. A total of 87,151 (44%) returned the completed questionnaire and formed the baseline cohort. Four years later (2009), 60,569 (69%) were successfully followed up, and of these, 42,785 (71%) were followed again in 2013.

2.1. Participant Selection

TCS members who completed all three questionnaires (2005, 2009, and 2013) were eligible for the current study (N = 42,785). Previous experience with this cohort suggests that around half of all TCS members invited to participate in sub studies respond [19]. In order to achieve our desirable sample size of ~1000 (see Statistical methods), we invited a random sample of 2400 TCS members to complete an additional mail-out dietary survey in 2015 expecting that approximately ~1100 participants would be successfully followed up.

2.2. Dietary Intake

Dietary intake was assessed in 2015 using the validated Thai National Health Examination Survey food frequency questionnaire (FFQ) [20]. The participants were asked to indicate the frequency of consumption of each food item on average with one of seven response categories ranging from "don't eat at all" to "more than once per day". FFQ responses for each item were converted into daily intake

equivalents as follows: "don't eat at all" = 0, "less than once per month" (0.5/30 = 0.02), "1–3 times per month" = 0.07, "1–3 times per week" = 0.28, "4–6 times per week" = 0.71, "once per day" = 1, or "more than once per day" = 2.5. Participants were excluded from this study if responses to >10% of food consumption items were missing while all of the other missing FFQ items were considered as not consumed [21]. All of the 44 food items were allocated into 30 separate food groups according to nutritional content, culinary use, and previous dietary pattern studies [17] (Table S1).

2.3. Socio-Economic Position

We used three measures of socio-economic position (SEP): monthly income, occupation, and highest level of attained education. Information on these measures was collected in the 2013 questionnaire. Occupation was included because personal monthly income is affected by earning disparities between Thai men and women [22]. Using occupation as a measure of SEP may help to detect differences in low and high SEP women that personal monthly income might not be able to discern due to the low number of women in the high income bracket. Data for all three SEP measures were collected in the 2013 follow-up questionnaire. Personal monthly income (Baht) was reported in categories and classified as: <10,000 (<295 USD), 10,001–20,000 (295–590 USD), 20,001–30,000 (>590–880 USD), or ≥30,001 (>880 USD). Level of attained education was categorized as having or not having a university degree. Data on occupation were reported in categories and further classified as: manual worker (e.g., labourers), office assistant, skilled worker (e.g., carpenter, hairdresser), professional (e.g., doctor, accountant), and manager (middle or senior).

2.4. Demographic Factors

Information on the location of current residence was collected in the 2005, and again in the 2013 follow-up questionnaires. In both questionnaires, residence was recorded as rural or urban. We combined the data for 2005 and 2013 and converted this measure into four categories based on residence reported in 2005 and in 2013: rural residence in both 2005 and 2013; rural residence in 2005, urban residence in 2013; urban residence in both 2005 and 2013; and, urban residence in 2005, rural residence in 2013.

2.5. Statistical Methods

Since dietary intake in this cohort varies substantially by sex, especially for transitional foods, we performed all of the analyses separately for men and women [23].

2.5.1. Dietary Patterns

Dietary patterns were identified using principle component analysis (PCA). We determined the number of patterns to retain based on their eigenvalues (>1.0) (pointing to factors explaining more of the total variance than each original variable), using scree plots, and according to the interpretability of the identified pattern. The retained patterns were then orthogonally rotated to obtain a simpler factor structure and enhance their interpretability [24]. Food items with an absolute factor loading >0.30 or <−0.30 were considered as substantial contributors. Patterns were named based on the food items with the highest factor loadings. We then calculated a standardized score for each participant by summing the consumption frequency for each food group and multiplying it by the factor loadings for each dietary pattern [25].

2.5.2. Socio-Demographic Predictors of Dietary Patterns

We used multivariable linear regression to assess the associations between socio-demographic measures in 2013 and dietary intake pattern scores in 2015. We estimated standardized coefficients (ßeta) and 95% confidence intervals (CI). We identified potential confounders using directed acyclic graphs (DAGs) and by including in the model covariates of interest that had at least a 10% effect on

the predictors of dietary patterns [26]. Variables of interest included education, income, occupation, and area of residence. The covariates modelled included age and an interaction term for education and income (education x income) to assess the potential modifying effect of income on the association between education and dietary pattern scores.

2.5.3. Sensitivity Analysis

For each of the four dietary patterns, we found that a few individuals had very high consumption scores. To determine the potential impact that these participants might have on the effect estimates, we reassessed the association between the socio-demographic predictors and the four dietary patterns without these individuals

2.5.4. Sample Size

Sample size for this study was determined by considerations that led us to recruit ~1000 participants. Generally, for PCA, between five to ten participants per item will provide an adequate sample size (in our study 150–300 participants) [27]. As well, power calculations indicate that a sample of 500 participants (i.e., men or women) with at least 20% in each socio-demographic group allow us to detect a statistically significant and substantial difference between two mean dietary scores of at least 0.4 standard deviations with a two-sided 5% significance level, and 80% power.

2.6. Ethics Approval

Ethical approval for the study was obtained from Sukhothai Thammathirat Open University Research and Development Institute (protocol 0522/10 (approved in 2004)) and the Australian National University Human Research Ethics Committee (protocols 2004/344 (approved in 2004)), 2009/570 (approved in 2009) and 2015/068 (approved in 2015). Informed written consent was obtained from all participants. All data were de-identified before analysis. We thank Professor Aekplakorn for permission to use the Thai National Health Examination Survey FFQ.

3. Results

3.1. Participants

Of the 2400 randomly selected TCS participants, 1090 (45%) completed and returned their dietary surveys. Of these, 15 (10 men, 5 women) did not respond to >10% of their FFQ questions, so they were excluded. Analyses were based on the remaining 1075 participants and comparisons are summarised in the supplementary Table S2. Those who completed the FFQ and those who did not respond were similar with respect to body mass index (BMI), area of residence, occupation, and income (all p-values > 0.2), although respondents were, on average, older ($p < 0.001$) and had higher levels of attained education ($p < 0.01$).

When compared to the female participants, male participants were older, had a higher BMI, and earned a higher monthly income ($p < 0.001$). Male participants were also more likely to work as senior managers than female participants ($p < 0.001$). Having attained a university education was more common in women than in men ($p < 0.01$). These results were statistically significant but the actual differences were not large.

Figure 1 shows the proportion of 2015 dietary survey participants consuming each food group per week by sex. Vegetables and white rice were the most commonly consumed food groups by all of the participants. As compared to women, men consumed higher proportions of white rice, fish, coffee, sugar-sweetened beverages, and fatty meat ($p < 0.05$). When compared to men, women consumed higher proportions of fruit, brown rice, milk, and soy milk ($p < 0.05$).

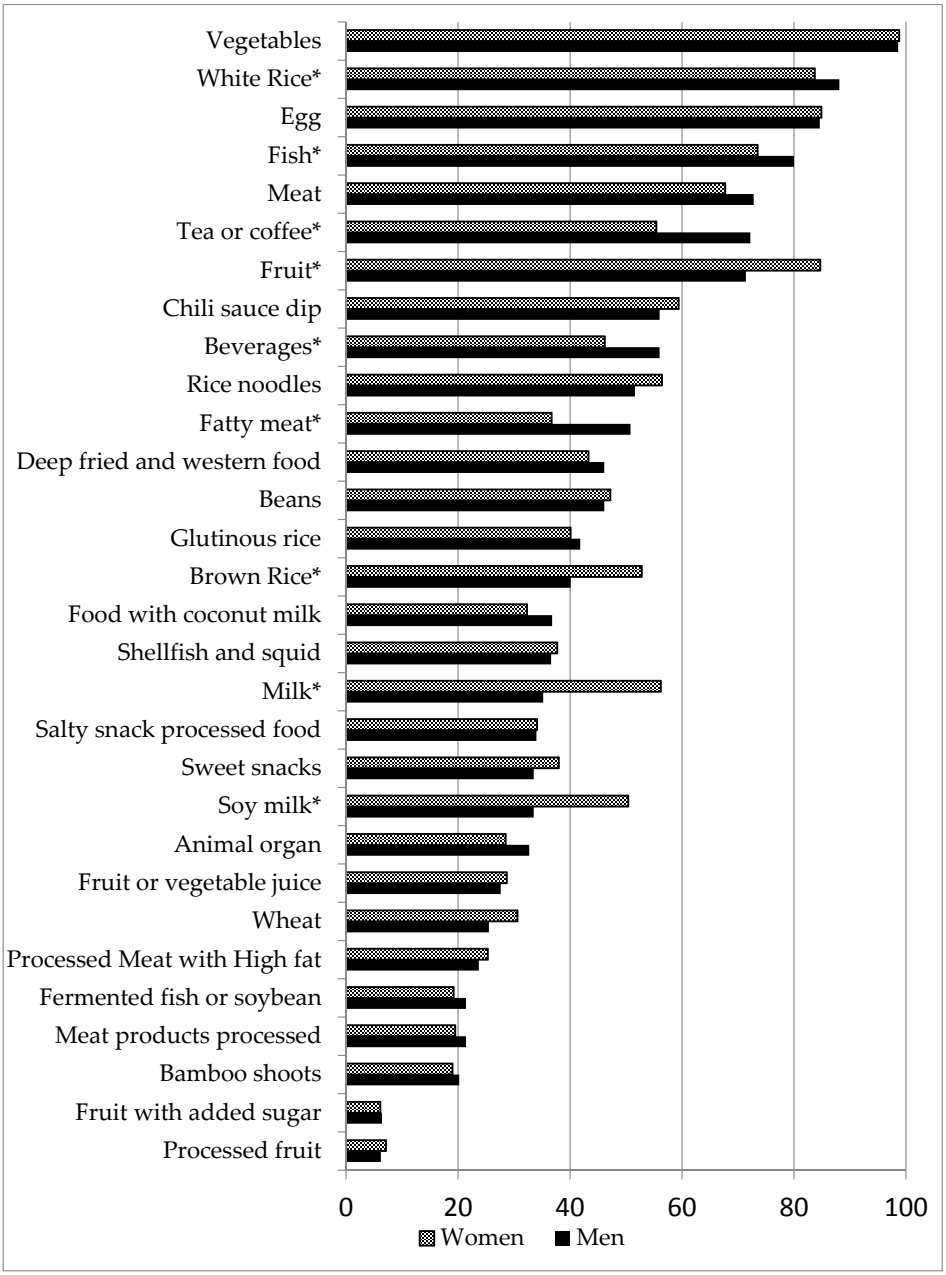

Figure 1. Percentage of Thai adults consuming each food group per week by sex. * χ^2 p value < 0.05 when comparing weekly food group consumption frequency by sex.

3.2. *Diet Patterns*

Four dietary patterns were identified both in men and women (Table 1). These patterns are named here as Healthy Transitional (soy milk, beans (legumes), and milk (in both sexes), fruit (only in men) and fish (only in women)); Fatty Western (fatty meat and deep fried and western food (in both sexes), and meat (only in men)); Highly Processed (fruit with added sugar, processed fruit (in both sexes), sweet snacks and processed meat products (only in men), and salty snacks, wheat and juice (only in women)); and, Traditional (fermented fish and soybean, glutinous rice, bamboo shoots, and chili dipping sauce). The Healthy Transitional and Fatty Western diets are both characterized by high protein availability and increased dietary diversity while the Highly Processed and Traditional diets are both characterized by high sugar and starch availability and lower dietary diversity. The total variance explained by these four patterns in men and women, was 37% and 36%, respectively.

Table 1. Factor loadings * for four dietary patterns identified among Thai adults.

Food Groups (Men)	Healthy Transitional	Fatty Western	Highly Processed	Traditional
Soy milk	0.41	-	-	-
Beans	0.37	-	-	-
Fruit	0.34	-	-	-
Milk	0.32	-	-	-
Brown rice	0.30	-	-	-
Wheat	0.30	-	-	-
Fatty meat	-	0.38	-	-
Deep fried and western food	-	0.36	-	-
Meat	-	0.34	-	-
Rice noodles	-	0.33	-	-
Food with coconut milk	-	0.30	-	-
Fruit with added sugar	-	-	0.49	-
Processed fruit	-	-	0.44	-
Sweet snacks	-	-	0.38	-
Meat products (processed)	-	-	0.35	-
Fermented fish or soybean	-	-	-	0.53
Glutinous rice	-	-	-	0.47
Bamboo shoots	-	-	-	0.40
Chilli dipping sauce	-	-	-	0.33
Dietary variance explained %	10.9	10.8	8.5	6.7
Food groups (Women)	**Fatty Western**	**Healthy transitional**	**Highly processed**	**Traditional**
Deep fried and western food	0.35	-	-	-
Fatty meat	0.35	-	-	-
Food with coconut milk	0.31	-	-	-
Soy milk	-	0.37	-	-
Beans	-	0.37	-	-
Fish	-	0.36	-	-
Milk	-	0.30	-	-
Processed fruit	-	-	0.44	-
Wheat	-	-	0.34	-
Fruit or vegetable juice	-	-	0.33	-
Salty snacks	-	-	0.31	-
Fermented fish or soybean	-	-	-	0.49
Glutinous rice	-	-	-	0.47
Bamboo shoots	-	-	-	0.46
Chilli dipping sauce	-	-	-	0.31
Dietary variance explained %	11.2	9.7	7.8	7.1

* Only factor loadings >0.30 or <−0.30 are displayed in the body of the table. These represent correlation coefficients between individual food groups and each dietary pattern.

3.3. Socio-Economic Position and Dietary Patterns

The multivariable-adjusted sex-specific associations between SEP and the four dietary patterns are shown in Tables 2 and 3. Among women, higher incomes of 20,001–30,000 or ≥30,001 Baht/month (vs. ≤10,000) were both associated with a lower Traditional diet score (ß = −0.62, 95% CI −1.06, −0.18) and (ß = −0.67, 95% CI −1.15, −0.19) and working as a manager or as a professional (vs. office assistant) were both associated with a lower Fatty Western diet score (ß = −0.60, 95% CI −1.14, −0.05) and (ß = −0.48, 95% CI −0.86, −0.11), respectively. Among men, a higher income was positively associated with a higher Healthy Transitional diet score, and working as a manual labourer was associated with a higher Fatty Western diet score; both ß coefficients were substantial (>0.5) but not statistically significant.

In women, having a university education (vs. not) was associated with a lower Highly Processed diet score (ß = −0.57, 95% CI −0.98, −0.17) and a higher Traditional diet score (ß = 0.42, 95% CI 0.03, 0.81). In men, education level was not significantly directly associated with any of the dietary patterns. However, income modified the association between education and the Highly Processed diet (*p* for interaction 0.03). At a low income of <10,000 Baht per month, having a university education (vs. not) was associated with a lower Highly Processed diet score (ß = −1.02, 95% CI −1.78, −0.25).

3.4. Urbanization and Dietary Patterns

The associations between urban residence and the four identified dietary patterns are shown in Tables 2 and 3. Among women, when compared to rural residence, urban residence was associated

with a higher Fatty Western diet score (rural-urban: ß = 0.55, 95% CI 0.02, 1.08; urban-urban: ß = 0.68 95% CI 0.32, 1.04) and a higher Highly Processed diet score (ß = 0.44, 95% CI 0.13, 0.75,) but with a lower Traditional diet score (rural-urban: ß = −0.60, 95% CI −1.04, −0.17; urban-urban: ß = −0.68, 95% CI −0.98, −0.39). Among men, as compared to rural residence, urban residence was associated with a higher Fatty Western diet score (ß = 0.59, 95% CI 0.20, 1.00), and a lower Traditional diet score (urban-rural: ß = −0.77, 95% CI −1.39, −0.15; rural-urban: ß = −0.74, 95% CI −1.21, −0.26; urban-urban: ß = −1.00, 95% CI −1.31, −0.68).

Table 2. Multivariable linear regression of socio-demographic predictors in 2013 and dietary intake pattern scores in 2015 in 486 Thai men.

Predictors	Beta Coefficients and 95% Confidence Intervals			
	Healthy Transitional	**Fatty Western**	**Highly Processed**	**Traditional**
Income (Baht/month)				
≤10,000	reference	reference	**	reference
10,001–20,000	−0.20 (−0.79, 0.40)	−0.09 (−0.68, 0.51)		0.06 (−0.39, 0.53)
20,001–30,000	−0.05 (−0.67, 0.57)	0.06 (−0.55, 0.68)		0.01 (−0.47, 0.49)
≥30,001	0.66 (−0.04, 1.36)	−0.16 (−0.86, 0.53)		−0.36 (−0.90, 0.18)
Education				
University	−0.35 (−0.82, 0.11)	−0.24 (−0.70, 0.22)		0.05 (−0.30, 0.41)
Education level by income (Baht/month)				
Below university	-	-	reference	-
<10,000, university	-	-	−1.02 (−1.78, −0.25)	-
10,001–20,000, university	-	-	0.07 (−0.54, 0.69)	-
20,001–30,000, university	-	-	−0.11 (−0.86, 0.64)	-
≥30,001, university	-	-	0.95 (−0.20, 2.09)	-
Occupation				
Manual worker	0.09 (−0.48, 0.67)	0.52 (−0.05, 1.09)	0.34 (−0.14, 0.82)	0.04 (−0.41, 0.48)
Office assistant	reference	reference	reference	reference
Skilled worker	0.26 (−0.44, 0.96)	0.19 (−0.50, 0.88)	0.26 (−0.32, 0.84)	−0.01 (−0.54, 0.54)
Professional	0.01 (−0.50, 0.51)	−0.07 (−0.57, 0.43)	0.03 (−0.39, 0.45)	−0.06 (−0.45, 0.33)
Manager	0.38 (−0.15, 0.92)	0.19 (−0.34, 0.72)	0.18 (−0.26, 0.63)	0.25 (−0.16, 0.66)
Urban residence				
Rural-rural	reference	reference	reference	reference
Urban-rural	−0.17 (−0.98, 0.63)	−0.18 (−0.98, 0.62)	−0.20 (−0.87, 0.46)	−0.77 (−1.39, −0.15)
Rural-Urban	0.44 (−0.18, 1.05)	0.29 (−0.32, 0.90)	0.24 (−0.26, 0.75)	−0.74 (−1.21, −0.26)
Urban-Urban	0.19 (−0.21, 0.60)	0.59 (0.20, 1.00)	0.14 (−0.19, 0.48)	−1.00 (−1.31, −0.68)

All Beta coefficients are adjusted for age and for each other. ** The *p* for interaction for education x income was statistically significant for the highly processed diet pattern and therefore the main effect associations between income and education with this pattern are not displayed.

Table 3. Multivariable linear regression of socio-demographic predictors in 2013 and dietary intake pattern scores in 2015 in 589 Thai women.

Predictors	Beta Coefficients and 95% Confidence Intervals			
	Healthy Transitional	**Fatty Western**	**Highly Processed**	**Traditional**
Income (Baht/month)				
≤10,000	reference	reference	reference	reference
10,001–20,000	−0.20 (−0.64, 0.24)	−0.01 (−0.45, 0.43)	−0.06 (−0.44, 0.31)	−0.20 (−0.55, 0.16)
20,001–30,000	−0.21 (−0.75, 0.33)	−0.22 (−0.76, 0.32)	0.26 (−0.20, 0.72)	−0.62 (−1.06, −0.18)
≥30,001	−0.37 (−0.96, 0.22)	0.03 (−0.56, 0.62)	0.48 (−0.01, 0.98)	−0.67 (−1.15, −0.19)
Education				
University	−0.02 (−0.51, 0.46)	−0.04 (−0.52, 0.44)	−0.57 (−0.98, −0.17)	0.42 (0.03, 0.81)

Table 3. *Cont.*

Predictors	Beta Coefficients and 95% Confidence Intervals			
	Healthy Transitional	**Fatty Western**	**Highly Processed**	**Traditional**
Occupation				
Manual worker	−0.22 (−0.76, 0.33)	−0.09 (−0.63, 0.46)	−0.15 (−0.61, 0.31)	−0.02 (−0.46, 0.42)
Office assistant	reference	reference	reference	reference
Skilled worker	0.18 (−0.69, 1.05)	0.09 (−0.78, 0.95)	0.05 (−0.68, 0.78)	−0.01 (−0.71, 0.69)
Professional	0.08 (−0.30, 0.47)	−0.48 (−0.86, −0.11)	0.06 (−0.26, 0.38)	0.08 (−0.23, 0.38)
Manager	0.28 (−0.26, 0.83)	−0.60 (−1.14, −0.05)	−0.13 (−0.59, 0.33)	0.26 (−0.18, 0.70)
Urban residence				
Rural-rural	reference	reference	reference	reference
Urban-rural	0.12 (−0.47, 0.70)	0.58 (−0.01, 1.16)	0.12 (−0.37, 0.62)	−0.22 (−0.69, 0.25)
Rural-Urban	0.08 (−0.46, 0.61)	0.55 (0.02, 1.08)	0.27 (−0.18, 0.72)	−0.60 (−1.04, −0.17)
Urban-Urban	−0.10 (−0.46, 0.27)	0.68 (0.32, 1.04)	0.44 (0.13, 0.75)	−0.68 (−0.98, −0.39)

All Beta coefficients are adjusted for age and for each other.

3.5. Sensitivity Analysis

The effect estimates were similar when we removed the 15 individuals (nine men and six women) with the high consumption scores (see Methods) so these individuals were retained in the main analyses. Similarly, excluding individuals with missing data for any FFQ items did not change the results.

4. Discussion

We assessed diets and their socio-demographic predictors in a prospective cohort of Thai adults. Using Principle Component Analysis, four major dietary patterns were evident: Healthy Transitional, Fatty Western, Highly Processed, and Traditional. For both sexes, high SEP associated with a lower consumption of unhealthy foods; urban residence associated with greater food diversity, but also with foods that have been shown to increase NCD risk in previous studies.

Some limitations should be considered when interpreting our findings. The FFQ used in our study documented intake frequency and we did not adjust for energy intake. Another issue to consider is the subjective nature of decisions that is required by the factor analysis technique; although, this method is data driven, and at several points during the analysis the investigators are required to make important decisions [24]. These include the consolidation of individual foods into food groups, determining the number of factors to retain, choosing the rotation method, and labelling the factors in interpretable ways [24]. To minimize subjectivity, we used our knowledge of Thai cuisine and previous dietary pattern studies to guide our construction of food groups. Scree plots and eigenvalues supported the statistical basis for retention of four dietary patterns.

Important strengths of this study include the prospective data collection and nationwide coverage of our sample of Thai adults. We used an FFQ that has been previously validated in the national Thai population and which has been used to determine dietary patterns and their association with health outcomes [17]. Furthermore, the TCS participants are ideal for studying the association between socio-demographic factors and patterns of dietary consumption in LMICs since this cohort is becoming urbanized, using education for self-improvement, and experiencing the health-risk transition ahead of their fellow Thais [15].

The four dietary patterns identified in our study are similar to those reported in both LMICs and HICs, and the total variance explained by these factors in men and women (37% and 36%, respectively) is similar to what has been reported in previous studies [17,28]. The Fatty Western and Highly Processed dietary patterns in our study resemble the "Western", "Unhealthy", "Convenience", or "Meat" diet patterns reported in LMICs [29,30] and HICs [13,31] since they are high in added sugars and saturated fat. These dietary patterns characterize the "degenerative" stage of the nutrition transition since they associate with increased NCD risk [3]. Some aspects of the Healthy Transitional pattern in our study resembles the "Prudent" or "Healthy" dietary patterns commonly reported in upper-middle

income [11,32] or HICs [33]. This pattern reflects a shift from a traditional diet (carbohydrate based) to one that is high in dietary quality and diversity. Unlike the "Western Diet", the Healthy Transitional pattern is associated with reduced NCD risk [33]. The Traditional dietary pattern is similar to the "Traditional" or "Carbohydrate" diet patterns reported in LMICs, with intakes high in dietary starches and low in dietary diversity [17,34].

In agreement with previous studies from upper-middle income countries [6,11,35] and HICs [13,36], we found that having a high SEP was associated with healthier and more diverse dietary patterns that reduce NCD risk. For example, women who earned a higher income were less likely to consume a traditional diet. Although the Traditional diet does offer various vitamins and minerals, it is also low in dietary diversity and high in starchy glutinous rice, which has been found to increase metabolic disease risk in Asian populations [17,37]. Although the association was not statistically significant, men who earned a higher income were more likely to consume a Healthy Transitional diet, characterized by the consumption of milk and brown rice, which are both associated with reduced risk of T2DM [38,39]. These findings support the nutrition transition theory that states that negative health behaviours reverse in the final stages of the transition and that this occurs first in high-SEP individuals [40]. Indeed, Thailand now has one of the highest gross national incomes (GNIs) among upper-middle income countries [14]. Younger Thais may already be exhibiting a "cultural resistance" to consuming western fast-food diets, with a higher resistance being reported among those with a higher education level [41]. Our findings highlight the need for public health efforts to target the promotion of healthy eating in low-SEP Thai adults.

Education was associated with the lower consumption of unhealthy dietary intake in both men and women, but in men, this effect was modified by income. Previous studies have found that income and education may have independent roles in dietary intake and health outcomes like obesity, and that in women, education has a stronger protective role than income [42–44]. In this cohort all of the participants had at least begun a university degree. Therefore, it may be that an independent association with education in men would only be apparent if there was larger variance in education levels between groups.

We found that female participants in this study consumed a lower proportion of high fat and highly processed foods (e.g., sugar sweetened beverages and fatty meat) than men. This finding has been consistently reported in the literature [11,45,46] and may be due to women's concerns with weight loss and body size [47]. However, women tend to adopt health promoting behaviours and better health outcomes more rapidly than men [48]. This sex-specific finding also reflects what commonly occurs in middle-income countries as they progress along the nutrition transition. Such a difference in men and women is well-recognized and healthy eating should be promoted in Thai men.

In both sexes, urban residence was associated with consumption of a greater diversity of foods (e.g., higher meat consumption and lower rice consumption), but also with foods that have been shown to increase NCD risk in previous studies, a common finding in LMICs [3]. We also found that in Thai women, migrating from a rural residence to an urban residence was associated with consuming an unhealthy diet. This could relate to the greater availability of highly processed and unhealthy foods in urban areas that may not be as widely available in rural areas. Indeed, in Thailand, the association between urbanization and NCD-promoting dietary patterns has been attributed to growth of the modern food retail sector (e.g., western supermarkets, convenience stores) in urban areas [49]. Over the past two decades, the rapid growth of the modern food retail sector has led to a substantial decrease in the number of fresh markets that are available in urban areas, including Bangkok [49,50]. Unlike fresh markets that sell fresh foods, modern food retailers sell inexpensive and highly processed food items and these are considered to be "more fashionable" than the traditional Thai food retail sector [51]. Increasing access to affordable and healthy food in urban areas should be considered a priority as part of the national NCD control efforts.

5. Conclusions

In this prospective nationwide study of Thai adults, we found strong and coherent evidence that socio-demographic factors are associated with dietary patterns. Our findings suggest that Thai adults are exhibiting an increasingly "developed" country pattern of diets with an increasing SEP. Thai policy makers need to promote consumption of a healthy diet, particularly in urban residents, in men, and in low-SEP Thai adults as a central part of the national NCD control efforts, especially for the prevention of T2DM and cardiovascular diseases.

Supplementary Materials: The following are available online at www.mdpi.com/2072-6643/9/11/1173/s1, Table S1: Food items and food groups derived from the food frequency questionnaire, Table S2: Participants versus non-participants in the 2015 TCS dietary survey.

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Author Contributions: K.P. devised the dietary study, analyzed all of the data, and wrote the paper. S.J., C.B., A.S. and S.S. assisted with the planning of the study and the construction of the dietary survey. C.D. and S.J. guided the analytical approach of this paper, supervised all analyses of the data and helped with the interpretation of the study findings. C.B. and V.Y. assisted with the interpretation of the 2013 cohort data and with the editing of the manuscript. A.S. and S.S. conceived and developed the cohort. All authors approved the final manuscript.

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Supplement 1: Food items and food groups derived from the food frequency questionnaire

Food group	FFQ food items
Meat	Beef, pork, chicken, duck meat without skin
Fatty meat	Beef, pork, chicken or duck with added skin
Processed meat (fatty)	Processed meat high in fat (i.e. sausage)
Processed Meat (salted)	Processed meat high in salt (i.e. dried/salted fish or meat)
Fish	Fresh and salt water fish
Shellfish and squid	Shrimp, shellfish, crab, squid
Animal organs	Liver from pig, duck or chicken
Egg	Egg
Beans	Legumes and their products (i.e. mung, soy, tofu)
White rice	White rice
Brown rice	Brown rice
Glutinous rice	Sticky rice
Rice noodles	Rice noodles
Wheat	White bread, wholemeal bread
Deep fried and western food	Deep fried pork, Pizza, hamburgers
Food with coconut milk	Curry style dishes (i.e. Tom Kha, red curry)
Fermented fish or soybean	Fermented salted fish, fermented beans
Chili sauce dip	Chilli sauces (i.e. nam prik)
Fruit	Sweet (i.e. Papaya, lychee) and non-sweet (i.e. green apple)
Fruit with added sugar	Candied fruit, fruit paste
Processed fruit	Dried, canned, pickled
Milk	Fresh milk, yoghurt,
Soy milk	Soy milk
Beverages	Sweetened milk, soft drink, energy drinks, sports drinks
Fruit or vegetable juice	Fruit or vegetable juice
Tea or coffee	Tea or coffee
Sweet snacks	Dessert (with sweet syrup, coconut milk, yolk), baked goods
Salt snacks (highly processed)	Potato chips, Instant noodles
Bamboo shoots	Bamboo shoots
Vegetables	Vegetables

Supplement 2: Participants *versus* non-participants in the 2015 TCS dietary survey

Characteristics in 2013	Non-participants* n (%)	Participants* n (%)	P value**
Total	1310 (55%)	1090 (45%)	
Sex			0.37
Men	572 (43.7)	496 (45.5)	
Women	738 (56.3)	594 (54.5)	
Age years			<0.001
Under 30	91 (7.0)	52 (4.8)	
30-39	629 (48.0)	450 (41.3)	
40 or over	590 (45.0)	588 (**54.0**)	
Body Mass Index			0.66
<23.0kg/m^2	632 (48.8)	548 (50.6)	
23.0-<25.0 kg/m^2	298 (23.0)	236 (21.8)	
≥25.0 kg/m^2	366 (28.8)	300 (27.7)	
Residence			0.95
Rural	576 (44.4)	481 (44.5)	
Urban	721 (55.6)	599 (55.5)	
Education			<0.01
No university education	311 (23.9)	199 (18.3)	
University education	989 (76.1)	886 (**81.7**)	
Occupation			0.51
Manual worker	192 (16.2)	142 (14.6)	
Office assistant	421 (35.5)	323 (33.2)	
Skill worker	66 (5.6)	57 (5.8)	
Professional	328 (27.6)	294 (30.2)	
Manager	190 (15.2)	158 (16.2)	
Income			0.18
≤10,000	291 (22.6)	246 (22.7)	
10,001-20,000	486 (37.7)	380 (35.1)	
20,001-30,000	305 (23.6)	246 (22.7)	
≥30,001	208 (16.1)	210 (19.4)	

*Numbers may not add to total sample size due to missing responses for some characteristics

**χ^2 comparing each baseline characteristic by participation status

8

DISCUSSION AND CONCLUSIONS

8 Discussion and conclusions

8.1 Overview

The body of work included in this thesis contributes to our understanding of the epidemiology of the emerging type 2 diabetes mellitus (T2DM) epidemic in Southeast Asia. It has adapted an eco-social model to identify potential local risk factors and investigate their actual associations with T2DM in the Thai population. This final chapter provides a synthesis of the key results presented in Chapters 3-7.

Section 8.2 reviews the findings and explores the implications; at the end of this section Table 8-1 is inserted as a matrix that connects the research questions, hypotheses, and objectives to the findings and implications. The subsequent Section (8.3) highlights the strengths and limitations of this research. The public health significance of this work is then discussed in Section 8.4 along with priorities for future research in this area (Section 8.5) and the overall conclusions (Section 8.6).

8.2 Key findings and implications

In this section of the discussion I summarize the key findings presented in the five published papers reproduced in Chapters 3-7. Focused on Thailand, these findings cover the validity of self-report, incidence and trends of T2DM, and its multi-level risk factors including emerging dietary patterns. As the findings and implications are considered, propositions are advanced to explain the noted trends or suggest specific actions.

8.2.1 Validity of self-reported doctor-diagnosed T2DM in Thai adults

The validation study of self-reported doctor-diagnosed incident T2DM in Thai adults participating in the Thai Cohort Study (TCS) was presented in Chapter 3. Overall, 82% of those who self-reported diabetes were confirmed to have doctor-diagnosed diabetes and 78% were confirmed to have doctor-diagnosed T2DM. Of those who reported having diabetes in two waves of follow-up, 96% were confirmed to have T2DM, based on physician diagnosis. The high accuracy of self-reported T2DM among TCS participants is consistent with findings from Caucasian populations, including studies conducted in highly educated cohorts (Field et al., 2001, Hu et al., 2001). Self-report in our cohort was more accurate than that reported in the few studies carried out in Asian cohorts (Goto et

al., 2013, Wu et al., 2000). The higher accuracy in our study is likely to be related to the make-up of our cohort. Unlike the few available Asian-based studies, our cohort is relatively young and has higher levels of attained education, two characteristics that have been reported to be associated with higher accuracy of T2DM self-report (Molenaar et al., 2007). In the TCS, the proportion of confirmed self-reported diabetes cases did not vary by socio-demographic characteristics, but the proportion of confirmed self-reported T2DM was lower in young women. Most of these TCS women were found to have had gestational diabetes and this suggests that studies which include young women should ask whether self-reported diabetes was related to pregnancy.

Despite differences in cohort structures and the methods used to validate self-reported diabetes in our study and in other validation studies, the general finding across studies is that the validity of self-reported diabetes is high (Goldman et al., 2003, Huerta et al., 2009, Wu et al., 2000). T2DM self-report is a valid method for assessing new cases of T2DM in Thai adults. This low cost method will be useful for assessing the trends and determinants of T2DM in the Thai population.

Proposition 1:

Self-reported doctor-diagnosed T2DM is a suitable low cost method to track trends and determinants in young to middle-aged, educated Thai adults.

8.2.2 Incidence and risk factors for T2DM in Thai adults

The research on T2DM incidence, SSBs, BMI, and dietary patterns adds to the knowledge base on the epidemiology of T2DM in Southeast Asia. Results are discussed together, organized according to the adapted eco-social model which connects incidence trends to risk factors in multiple levels.

8.2.2.1 T2DM incidence

The incidence of T2DM in the TCS over an eight-year period between 2005 and 2013 was 177 per 10, 000 (95% CI 164 to 190). Comparisons with other estimates for Thailand and for other countries are difficult because of potential differences in population sampling, age structures, attrition and diagnostic methods. However, our sex and age-specific estimates suggest that the incidence of T2DM in TCS members is higher than

Caucasian populations from North America (Geiss et al., 2014, Lipscombe and Hux, 2007) and Europe (Chevreul et al., 2014, Holden et al., 2013, Bonora et al., 2004). TCS findings on T2DM incidence are comparable to reports for populations from LMICs including Bangladesh (Asghar et al., 2011), China (Hsu et al., 2012), the Philippines (Karter et al., 2013), and Iran (Janghorbani and Amini, 2012). Notably, TCS estimates are lower than reported rates for Indigenous populations (e.g. Pima Indians) (Pavkov et al., 2007), Pacific Islanders (Karter et al., 2013), Mauritians (Söderberg et al., 2004), and South Asian populations from India (Lele, 2008).

Overall, all these findings are not surprising given that in recent years T2DM incidence rates in HICs in the west including the UK, Denmark, Italy and the US appear to be stabilizing (Jaacks et al., 2016, Maruthur, 2013) while rates in LMICs (including Thailand) have been increasing. Several published reports suggest that the plateauing trends in incidence rates in HICs relate to increased public health efforts and shifts in the prevalence of underlying risk factors in the population (e.g. decreases in SSB consumption in recent years) (Gregg, 2017). While it is likely that some of the rate increases noted in LMICs are due to increased surveillance of T2DM and improved survival in those with T2DM, the changing risk factors identified in this study (including urbanization, aging, obesity, and lifestyle behaviours) are likely to be the major contributors for this increase (Maruthur, 2013).

In the TCS, a higher incidence of T2DM ($p<0.001$) was noted in men (249 per 10 000 in men versus 119 per 10 000 in women). This is consistent with the higher incidence in men noted in three previous Bangkok-based incidence studies and with other studies from both LMIC and HICs (Asghar et al., 2011, Chen et al., 2012b, Bonora et al., 2004). Different sex-specific T2DM findings have been reported in the National Health and Examination Surveys (NHES) in Thailand (conducted between 1991 and 2014) with a higher prevalence of T2DM noted in women (Aekplakorn et al., 2016). However, in the most recent NHES, Thai women with high levels of education had a lower prevalence of T2DM than highly educated men (Aekplakorn et al., 2016). As noted in the TCS, continued economic development may protect against T2DM and may benefit women before men.

Proposition 2:

TCS women are already experiencing lower rates of T2DM than their male counterparts. This trend is likely to expand in the population as Thailand progresses through the health-risk transition.

8.2.2.2 Biological risk factors

BMI was the largest risk factor for T2DM in the TCS. Indeed, two-thirds of all T2DM cases in the TCS could be attributed to overweight and obesity. Direct population attributable fraction comparisons across populations are difficult due to differences in the prevalence of overweight and obesity, T2DM rates, BMI cut-points, and variables included in the models. Nevertheless, our findings are relatively consistent with the few studies that have assessed the proportion of T2DM cases attributed to overweight and obesity in HICs (Davin et al., 2012, Laaksonen et al., 2010). Reducing the prevalence of obesity in Thai adults could greatly reduce the rise of T2DM incidence in the Thai population. I estimated that a hypothetical 5% reduction in the prevalence of obesity (BMI $\geq$25 kg/m^2) would result in a reduction of some 13,000 cases (about 13%) of T2DM annually in the national Thai population (Chapter 6).

Age and BMI associations with T2DM in TCS participants differed to findings from Caucasian populations. For example, risk of T2DM in the TCS increased at a relatively low age (odds of T2DM when aged 30-39 were already doubled - Chapter 4) and was much higher than the T2DM risk reported at the equivalent BMI levels in Caucasian populations (Misra, 2015, Hsu et al., 2015, Aekplakorn et al., 2006b, Chiu et al., 2011). This is consistent with studies conducted in Asian cohorts (Chiu et al., 2011, He et al., 2015). Compared to a reference of 20.00 kg/m^2, T2DM risk was increased with a BMI of 21.60 kg/m^2 and 20.03 kg/m^2 in Thai men and women, respectively. Differential associations between body size and T2DM risk for Asian and Caucasian populations may reflect ethnic differences in body composition (Deurenberg et al., 2002). Compared with Caucasians, for body composition, Asians are 'metabolically-disadvantaged', with lower lean mass and higher abdominal and visceral fat (Chan et al., 2009). Indeed, at any given BMI, Asians are likely to have more abdominal and visceral adiposity than Caucasians and thus an increased risk of insulin resistance and T2DM (Deurenberg et al., 2002).

Epigenetic programming may also play a role in predisposing Asian populations to greater deposition of visceral fat (Chan et al., 2009). Indeed, babies under-nourished in utero experience 'catch up growth' later in life and this has been associated with a predisposition to storing visceral fat and increased insulin resistance at lower levels of body weight (Yajnik, 2004, Tchernof and Després, 2013). Asian populations have experienced many generations of under-nutrition before experiencing the accelerated nutrition transition currently underway in much of developing Asia. As a result, some Asian populations may be increasingly predisposed to storing visceral fat and having increased insulin resistance at low levels of adiposity (Orsini and Greenland, 2011, Chan et al., 2009). Furthermore, potential effects of epigenetic programming may be particularly intensified when there is a strong mismatch between intrauterine environment and later life environments (Li et al., 2010), such as the obesogenic environment that is wide spread in Thailand today.

Sex also played a role in the BMI-T2DM association in TCS members. As in previous studies (Abdullah et al., 2010, Huerta et al., 2013) it was found that for a given level of BMI, T2DM risk was substantially higher in TCS women ($p<0.05$). This sex-specific finding may relate to differences in body composition and hormones between men and women (Ding et al., 2006). For instance, men have higher concentrations of testosterone than women and testosterone has been associated with increased lean body mass and decreased adiposity. Moreover, testosterone plays a role in decreasing inflammatory cytokines, and thus may help with decreasing insulin resistance (Ding et al., 2006).

Overall, the BMI findings from this thesis suggest there is a need to use lower BMI cut-points to define T2DM risk in Southeast Asia. A BMI cut-point of 22 kg/m^2, one point lower than the current 23 kg/m^2, could be justified for defining T2DM risk in Thai adults. In addition, healthy weight should be promoted differently in Thai men and women. This could include using different BMI thresholds for Thai men and women when calculating a diabetes risk score.

Proposition 3:

T2DM risk associated with body size in the Thai population could be operating at a lower BMI than currently accepted. If confirmed, the recommendations for relating BMI to T2DM risk need to change.

8.2.2.3 Behavioural risks

The TCS men are engaging in more of the adverse lifestyle behaviours that associate with T2DM risk compared with the women. For example, the men have a higher prevalence of smoking, are less physically active, and consume alcohol and unhealthy foods regularly ($p<0.001$); these behaviours are all associated with increased weight gain, insulin resistance and poor cardiovascular health (World Health Organization, 2016). Conversely, for Thai women in our study, smoking and alcohol consumption is uncommon while the consumption of healthy foods is widespread. This is also a common finding in the literature and may relate to women's concerns with weight (Wardle et al., 2006) and/or to social or cultural norms (Pampel et al., 2010). As well, evidence from upper-middle income countries including Iran (Rezazadeh et al., 2010), Brazil (Arruda et al., 2014), China and Mexico (Monteiro et al., 2004) suggests that women tend to adopt healthy behaviours more rapidly than men (Monteiro et al., 2004) and that this occurs at the later stages of the health-risk transition. This is well recognized and thus, given our findings, public health interventions need to target T2DM risk factors differently in Thai men and women. As part of this health promotion work, healthy eating and cessation of smoking and alcohol consumption should be promoted in men. In addition, trends in smoking and alcohol consumption in women should be monitored to ensure that low rates are maintained.

The men in this cohort also had a higher consumption of sugary-sweetened beverages (SSBs) than the women ($p<0.001$). Despite, the higher exposure in men, consumption of SSBs was only associated with increased risk of T2DM in women. Other studies have also shown that frequent SSB consumption increases T2DM risk in women (Palmer et al., 2008, Schulze et al., 2004, Eshak et al., 2013). Most studies have found significant associations between SSB intake and increased T2DM risk and those that have not were either conducted in older cohorts or only in men (Malik et al., 2010). SSB consumption is less common in older populations so it is possible that the prevalence of consumption

was too low to detect an association. It may be that this sex-specific association is explained by women's lower energy needs (Wolfe, 2006). Women generally have less muscle mass than men and thus lower energy needs so similar SSB intakes in men and women would contribute to a larger proportion of women's energy intakes (Eshak et al., 2013). Therefore, it is possible that any association between SSBs and T2DM in men is only apparent at very high levels of SSB consumption.

While it might be expected that SSBs contribute to T2DM risk by boosting caloric intake and increasing BMI, we found that obesity only mediated a moderate proportion (23%) of the association between SSB intake in 2005 and T2DM incidence in 2013 in women. These findings are consistent with what has been reported in Caucasian populations (Fagherazzi et al., 2013, De Koning et al., 2011b) and one other Asian population (Odegaard et al., 2010) and suggest that SSB intake increases the risk of T2DM independently of weight gain and obesity in Thai adults. High glycaemic loads from SSBs may lead to repeated high insulin demand and this can contribute to compromised beta (β) cell function (Ludwig, 2002). This SSB effect may be compounded in LMIC Asian adults who may have experienced under-nutrition during early life. They may have under development of β cell mass increasing risk of T2DM later in life independently of weight gain or obesity (George et al., 2015), particularly with exposure to high energy dense foods like SSBs (Ma and Chan, 2013, Li et al., 2010).

I estimated that about 1% of T2DM in men and 5% in women could be attributed to daily SSB intake. Assuming that the association between SSB intake and T2DM is causal an estimated 1500 T2DM cases in men and 2700 in women per year that may have been prevented in the national Thai population if daily SSB consumption was avoided. Similar findings have been reported in Caucasian populations with population attributable fractions ranging from 3.9% to 12.9% (Imamura et al., 2015).

These thesis results highlight the need for public health efforts to promote the reduction of SSB consumption in the national Thai population, particularly in women. The local evidence can guide public health efforts aimed at preventing increasing T2DM incidence in Southeast Asian populations. As SSBs have no nutritional value and do not protect against disease they are an ideal target for public health efforts. Taxing SSBs, banning SSB promotion, and public education programs are useful measures to reduce the

consumption of sugary drinks (Popkin and Hawkes, 2016) and have been shown to be successful in reducing tobacco consumption in Thailand (Sangthong et al., 2011) and globally (Scollo et al., 2003). Thailand has very recently brought in a sugar tax and the findings from this work were used as part of the local evidence to advocate for this tax.

Proposition 4:

Interventions for epidemic T2DM in Thailand should target SSBs, smoking, alcohol consumption, and unhealthy diets using Thai experience in health promotion.

8.2.2.4 Socio-demographic risks

The multi-level eco-social model I used to assess the upstream risk factors for T2DM in the Thai adults involved in the TCS included several socio-demographic measures. These were area of residence during childhood and at 2005 baseline, change in area of residence over the eight-year follow-up, education, occupation, and personal monthly income.

Examination of the associations between area of residence and T2DM risk showed that for both sexes, living in an urban area of residence increased the risk of having unhealthy dietary patterns and T2DM. Research from India, China, Bangladesh, Malaysia, Vietnam, the Philippines, and Iran have all found that urbanization is associated with increased risk of T2DM (Asghar et al., 2011, Harati et al., 2009, Chen et al., 2012b, Soria et al., 2009). It is likely that the association between living in an urban area of residence and T2DM risk reflects the greater exposure to various T2DM risk factors found in urban settings. For example, the rapid growth of the modern food retail sector has led to a substantial decrease in the fresh food markets available in urban areas and a large increase in the number of retail outlets that sell highly processed and inexpensive food items (Kelly et al., 2015). Furthermore, living in an urban residence has been associated with decreased physical activity, increased use of labour saving devices, higher rates of smoking, and greater alcohol consumption (Lim et al., 2009). Urban area of residence is a considerable risk factor for T2DM in Thai adults and therefore public health efforts aiming to control the T2DM epidemic in Thailand will need to ensure the urban environments are suitable for promoting the health of urban Thais. This may require further research to assess which aspects of urban planning policies that have been used in other countries (Rydin et al.,

2012) can be best adapted and implemented to promote the health of the urban residents in Thailand.

Proposition 5:

Increasing access to healthy food in urban areas will help to improve dietary patterns and reduce T2DM.

One of the striking findings from the work in this thesis was that different socio-economic factors were associated with T2DM risk in men and women. In men, but not in women, higher income and education were associated with increased T2DM risk. Conversely, in women, high SEP was associated with lower T2DM risk (Chapter 4). Moreover, we found that in women, having a high paying occupation and a high monthly income were associated with consuming a healthier diet, while in men these associations were less clear (Chapter 7). Education was associated with lower consumption of unhealthy foods in men and women, but in men this effect was modified by income. Previous studies suggest that income and education may have independent roles in dietary intake and health outcomes and that in women, education has a stronger protective role than in men (Monsivais and Drewnowski, 2009, Araujo et al., 2014, Monteiro et al., 2004, Monteiro et al., 2001).

Thai Cohort Study women are exhibiting 'developed country' dietary patterns and decreasing T2DM risk with increasing SEP, while men are exhibiting a 'developing country' pattern of increasing risk of T2DM with increasing SEP. As well, a lower prevalence of T2DM is already being noted among Thai women with high levels of education in the latest NHES (Aekplakorn et al., 2014). These findings support the nutrition and epidemiological transition theories that suggest that as a country enters the later stages of economic development, negative health behaviours reverse, and this occurs first in high-SEP individuals (Popkin and Gordon-Larsen, 2004). Our findings also suggest that public health interventions should target T2DM risk factors differently in Thai men and women.

A growing body of literature from upper-middle income countries suggests that as LMICs enter the later stages of economic development, the SEP-obesity relationship (Monteiro

et al., 2001, Soria et al., 2009, Yoon et al., 2006, Monteiro et al., 2004, McLaren, 2007, Pampel et al., 2012), and the social patterning of dietary intake reverses. Then higher levels of obesity and unhealthy consumption transfer to low SEP individuals, as seen in developed countries (Mayén et al., 2014), and this occurs in women first.

Proposition 6:

Targeting the risk factors identified in proposition 4 differently in men and women will help combat the T2DM epidemic in Thailand.

Table 8-1 Summary of research findings

Objective	Research question	Relevant hypotheses	Main findings
1. To validate self-report for detecting the disease in the population	1. *How valid is self-reported doctor-diagnosed T2DM?*	$1H_1$:*Self-reports of doctor-diagnosed T2DM are valid in Thai adults* $1H_2$: *Self-reports of T2DM can be used to asses trends and determinants in T2DM*	***Chapter 3*** • Self-reports of doctor-diagnosed T2DM are valid in Thai adults • Validity of self-report is similar across socio-demographic characteristics • Repeated self-report eliminates the need for further validity testing when assessing doctor-diagnosed T2DM • Self-reported T2DM needs cautious interpretation in young women who may report gestational diabetes ***Implications*** • Self-reported incident T2DM can be used to asses trends and determinants in T2DM in young educated Thai adults
2. To analyse the disease incidence and associated risks	2. *What is the incidence and what are the risk factors for T2DM?*	$2H_1$: *The incidence of T2DM in Thai adults is comparable with other countries undergoing a transition* $2H_2$: *Changes that have accompanied the health-risk transition are posing a T2DM risk*	***Chapter 4*** • The eight-year cumulative incidence of T2DM in Thai adults was 177 per 10,000 (95% Confidence Interval 164-190); with incidence rate higher in men (249 versus 119, per 10,000). • Changes that have accompanied the health-risk transition are posing a T2DM risk • Males are engaging in more health-risk behaviors and are exhibiting a 'developing country' pattern of T2DM risks • Thai women are likely to be in the advanced stages of the health-transition ***Implications*** • Public health interventions need to target the risk factors of T2DM differently in males and females • The focus of public health efforts should be on obesity, smoking, and alcohol, particularly among men

3. To assess the direct and obesity-mediated effects of sugar-sweetened beverages	3. *How do sugar sweetened beverages influence T2DM risk?*	$3H_1$: *Frequent SSB intake increases the risk of T2DM in Asian adults* $3H_2$: *Obesity mediates a proportion of the SSB-T2DM* $3H_3$: *SSB intake increases T2DM risk independent of obesity*	***Chapter 5*** • Frequent SSB intake increases the risk of T2DM, particularly in women • Obesity mediated a moderate proportion of the SSB-T2DM relationship (23%) • SSB intake may also increase T2DM risk through mechanisms independent of weight gain and obesity ***Implications*** • Public health efforts should promote reductions of SSB consumption - particularly in women • Increase awareness that SSB consumption can increase T2DM risk in Thai adults independently of weight gain and BMI
4. To investigate the relationship between BMI and T2DM, and calculate population attributable risk	4. *What is the relationship between baseline body mass index and incidence of T2DM in men and women in transitional Thailand*	$4H_1$: *BMI increases T2DM risk at a cut-off <25kg/m²* $4H_2$:*Over half of T2DM in Thai adults is attributed to excess weight*	***Chapter 6*** • Diabetes risk is increased at BMI levels below those currently recommended as health for Southeast Asian populations • Over 60% of diabetes in Thai adults could be attributed to overweight and obesity • A 5% reduction in obesity prevalence could prevent 13,000 diabetes cases annually – a reduction of about 13% ***Implications*** • A BMI cut-point of 22 kg/m² would be justified for defining T2DM risk in Thai adults, particularly in Thai women. • Lowering obesity prevalence would greatly reduce T2DM • Public health action and response may be required at lower BMI levels to help curb the T2DM epidemic in Thailand • Public health interventions should target the promotion of healthy weight differently in Asian men and women

5. To determine the association between upstream T2DM risk factors and dietary patterns	5. *How do socioeconomic position and urbanization status associate with dietary patterns in Thai adults?*	$5H_1$: *Women are more likely to follow a diet that reduces T2DM risk.* $5H_2$: *High SEP associates with a healthier dietary pattern in Thai adults* $5H_3$: *Urbanization associates with dietary patterns that promote T2DM risk*	***Chapter 7*** • Thai women were more likely to consume foods that prevent T2DM risk than Thai men. • High SEP associated with a lower consumption of unhealthy foods • urban residence with transitional diets including patterns associated with diabetes and cardiovascular disease ***Implications*** • Thai adults are exhibiting a 'developed' country pattern of dietary consumption with increasing SEP • Increasing access to affordable and healthy food in urban areas should be considered a priority as part of the national T2DM control efforts • Thai policy makers need to promote consumption of a healthy diet, particularly in urban residents, in men, and in low-SEP Thai adults

8.3 Strengths and limitations

The associations observed in this work need to be considered within the potential limitations of the methods and data used in this thesis. As highlighted in Chapter 2, all T2DM outcome data were ascertained using self-report. Therefore, there may have been some misclassification of T2DM. Indeed, we found that ascertaining T2DM through self-report led to some error in the classification of cases, resulting in an over estimation of T2DM incidence as shown in Chapter 3. However, the findings from our diabetes validation study suggest that the validity of T2DM self-reports were high and that misclassification of self-report became negligible (4%) once two waves of self-report data were considered.

The method used to confirm self-reported T2DM was physician telephone interviews, a method that may not be considered as the 'gold standard'. Accessing medical records that contain blood measures may have been a better method for confirming self-reported doctor-diagnosed T2DM but to do this we would have needed to gain access to medical records from across numerous health facilities and health professionals across Thailand. This was not feasible for such a large nationally dispersed cohort. For this thesis, we validated T2DM based on self-report of doctor-diagnosed T2DM using physician telephone interviews. This method may have resulted in some misclassification. Participants who have been told by a doctor that they have T2DM, and are probably treating their condition, would be more likely to remember their health condition and report their health status. As well, participants with diabetes who have not been diagnosed with T2DM by their doctors will report not having doctor-diagnosed T2DM. This would lead an under estimation of T2DM incidence. However, this is unlikely to have a large effect on T2DM trends and associations over time. People with undiagnosed diabetes are most likely to be at an earlier point in the natural history of this chronic disease but with the same risk factors as those manifested after diagnosis.

All exposure data were collected using self-report. Therefore, there may be some misclassification of the exposure measures. For instance, studies of self-reported weight and height have consistently found that self-reported height is commonly over estimated, while self-reported weight is often under estimated (Connor Gorber et al., 2007). Such misclassification of weight and height is likely to lead to an under estimation of BMI.

Misclassification of overweight and obese individuals into lower BMI categories would likely bias associations of BMI with increasing T2DM risk (Spencer et al., 2002). However, this misclassification is more common among older individuals and those with a larger body size. TCS participants are on average younger and have smaller body size than the national Thai cohort. Furthermore, validation studies that were conducted for some exposure variables in the cohort (i.e. height and weight) showed that self-report data in TCS participants were accurate and reliable (Lim et al., 2012).

Compared with the national Thai population, our cohort is younger, has higher levels of education, and a higher proportion of adults living in urban areas. Therefore, it is possible that the high validity of self-reported doctor-diagnosed diabetes in our cohort may be less applicable to the national population, which on average is older and has a lower level of attained education. Furthermore, the younger age of our cohort may have led to a lower overall T2DM incidence than in the national population. However, we expect that our age-specific rates are likely to be more generalizable than the overall rates.

Given that all the data used for this research were observational, residual confounding from unmeasured factors may be of concern. For example, SSB consumption, alcohol intake and smoking may be measured markers of an overall unhealthy lifestyle. Some of the effects of these exposures on T2DM risk in our study may be due to unmeasured confounding by other factors that associate with an unhealthy lifestyle. However, TCS investigators collected information on many potential confounders and these were considered during analyses. Moreover, the findings are consistent with the literature.

Loss to follow-up was substantial with about 50% of the baseline cohort followed up in 2013. Participants who were younger, had a lower BMI, had lower levels of education and income, who consumed SSBs regularly, and who smoked regularly at baseline were less likely to complete the two waves of survey follow-up. However, the actual differences in the drop-outs compared to participants was not large. Loss to follow up of participants with a lower T2DM-risk profile (young and underweight participants) may have led to selection bias, due to a higher retention of participants who are older and have larger body sizes. Higher retention of older participants and those with a larger body size may have led to some minor over-estimating of T2DM incidence. Conversely, loss to follow up of participants with a higher T2DM-risk profile (regular smokers and regular

SSB consumers) may have led to selection bias, due to a higher retention of participants who did not smoke and who did not consume SSBs regularly. Greater retention of participants who did not smoke and did not consume SSBs regularly may have led to an under estimation of T2DM incidence. However, it is likely that the effects of attrition on our relative estimates are small because participants who were lost to follow up in 2009 and/or in 2013 were similar in many respects, including their dietary behaviours (e.g. fruit, vegetable, and alcohol consumption), sex, and area of residence at baseline. Furthermore, the associations between BMI, SSB consumption, smoking, age, income and education with T2DM in the first four years (70% retention of baseline cohort) were similar to those for the eight-year follow-up (50% retention) indicating that bias was unlikely to have affected our results to a great extent.

Our data suggest that the probability of being followed-up in 2013 was associated with participants' baseline characteristics. It is likely that we lost contact with some cohort members because of the 'healthy volunteer' effect commonly reported in cohort studies (Webb and Bain, 2010) and/or because they would have graduated from the University and moved for employment opportunities. Because our cohort is younger, it is unlikely that many participants would have passed away or become too ill from T2DM to be followed-up, making it unlikely that attrition was the result of incident T2DM in this cohort.

Major strengths of this research include its cohort size, nationwide coverage, and longitudinal design. Previous studies have attempted to assess the burden and drivers of the emerging T2DM epidemic in transitioning Southeast Asian populations but most have been cross-sectional, limited in size, and/or mostly focused on assessing lifestyle behaviours. This research used a multi-level eco-social model to assess the upstream (geographical and socioeconomic) and downstream (behaviours including smoking, alcohol consumption, sugary beverage consumption, and increasing levels of overweight and obesity) factors driving the T2DM epidemic in Thailand. The prospective data and longitudinal design of this study with multiple repeated measures of exposures and confounders enabled calculation of T2DM incidence and investigation of local environmental and behavioural factors creating the T2DM risk.

Paradoxically, one of the main strengths of this research lies in one of its limitations - the differences between the characteristics of the adults involved in the TCS and the national Thai population. Thai Cohort Study participants are ideal for studying the effects of changing health-risks on T2DM. Although they represent the national population well in terms of geography and socio-economic status, they are also embracing the socio-economic changes underway in Thailand ahead of their fellow Thais. Indeed, rising education levels and rapid urbanization are major components of the health-risk transition, and these adults are already more urbanized and more educated. The findings from this thesis provide useful foresight regarding future national trends in T2DM and give a better understanding of the multi-level drivers of the T2DM epidemic in Thailand. Identified T2DM health-risks from this research will also likely benefit other Southeast Asian countries in the region, where data may be sparse, by helping them to develop appropriate public health interventions and policies to prevent T2DM and as they move through a similar health-risk transition.

8.4 Public health significance

The number of people living with T2DM in LMICs in Southeast Asia has reached epidemic proportions and is expected to keep rising with increasing life expectancy. Rapid economic growth, urbanization, and environmental changes are leading to an increased prevalence in health-risks including the increased consumption of highly processed food items, decreased levels of physical activity, and overweight and obesity. Identifying local-risk factor dynamics of the T2DM epidemic in developing Southeast Asian countries is necessary to produce the information needed to reduce the disease burden and prevent additional increases.

Thailand has one of the most influential economies in the Southeast Asian region, rapid urbanization rates, and a growing T2DM epidemic. I adapted an eco-social model to assess T2DM multi-level drivers. The health-risk factors included in the model capture the complex interplay between the distal or ‘upstream’ determinants (including geographical and socioeconomic) and the proximal or ‘downstream’ determinants (including age, BMI, and health behaviours) of T2DM in the Thai population. Indeed, results from this research show that downstream, transitional behaviours (including smoking, alcohol consumption, sugary-beverage consumption, and increasing levels of

overweight and obesity) are increasing T2DM risk. As well, upstream socio-demographic changes (including area of residence, occupation, and income levels) are affecting T2DM risk by interacting with downstream risk factors. For example, living in an urban area of residence associated with higher consumption of unhealthy dietary patterns in Thai men and women and the effect of an urban residence on T2DM appeared to work primarily through obesity. These associations demonstrate the links between behaviours, health-related outcomes, environment, and T2DM risk in Thailand.

Using a number of epidemiological methods, this body of research has provided new information on T2DM risk factors in Southeast Asian populations. Using restricted cubic splines (Chapter 6), this research found that the risk of T2DM in Thai adults was already increased at BMI levels considered to be in the healthy range for Asian populations. This information is very significant for Thailand, and provides local evidence of the need to use lower BMI cut-points when defining T2DM risk in public health policy and practice. Furthermore, by using a counterfactual mediation analysis to decompose the SSB-T2DM association (Chapter 5), this research provided evidence that SSB intake increases the risk of T2DM in Asian populations, both through and independently of weight gain or obesity. This information has refined and expanded local evidence for advocacy and was provided for the Thai government during discussions about an excise tax on sugar, which was implemented in September 2017.

8.5 Where to next

This work has identified the modifiable risk factors that need to be targeted to control the widespread T2DM epidemic in Thailand. It has also identified current knowledge gaps and additional research opportunities in this area.

Three transitional dietary patterns were identified that differed to the traditional Thai diet in TCS members. Given the substantial role that diet has for the control of blood sugar, further research is required to determine how these emerging diet patterns, and their temporal trajectories, associate with T2DM risk; and what aspects of this dietary change may be beneficial for preventing T2DM.

As discussed in Chapter 5, targeting SSB consumption can help prevent a national increase in the incidence of T2DM. Political measures like taxation have been

implemented in other countries as a form of targeted action to reduce the consumption of SSBs and very recently in Thailand. Previous performance of the Thai government in banning tobacco promotion has been successful for reducing tobacco use (Sangthong et al., 2011) and this experience suggests that parallel actions would be feasible for reducing SSB consumption. Further research is required to assess the effect of the newly implemented sugar tax on reducing SSB purchase and consumption in Thailand.

The findings from this work indicate that the women in this cohort appear to be at the later stages of the health-risk transition, as is commonly seen in high-income countries. Why women adopt health-promoting behaviours more rapidly than men in LMICs has not yet been determined. Further work is required to assess the determinants of adopting health-promoting behaviours in LMIC men and women.

We hypothesize that the large associations between BMI and T2DM in Thai adults may in part be explained by ethnicity, but may also relate to the prolonged exposure to living in an urban area, and the large mismatch in environments for adults who were under-nourished during their early life. There are limited data on T2DM incidence in Thai children and adolescents in Thailand. Thai children and adolescents growing up in Thailand's current economic state are likely to have been adequately nourished in-utero and to have experienced a similar environment in utero and in early life. Therefore, assessing T2DM and its risk factors in this younger group will help shed light on the body size-T2DM associations in Asian populations. This will help us to understand how much of the very large BMI-T2DM association in this population may be due to the effects of foetal programming, and/or to the effects of environment rather than ethnic predisposition to body composition. Data from a younger group will also help to identify ideal intervention points throughout the life course.

Thai food culture and knowledge is highly valued among Thai nationals and a 'cultural resistance' to western food products has already been identified among younger Thai adults with higher education levels (Seubsman et al., 2009). Further research is required to assess how pride in Thai culture can be utilized to devise a sustainable T2DM public health intervention for Thai adults.

8.6 Conclusions

The findings from this thesis contribute to better understanding of the epidemiology of T2DM emerging in Southeast Asia. Type 2 diabetes mellitus incidence in Thailand is high and the health-risk transition appears to be in its middle stages. With rapid urbanization and the prevalence of health-risk behaviours and obesity continuing to grow in Southeast Asia, we can expect that T2DM incidence will increase in the coming decades, with the majority of the growing burden occurring in men and in those with a low socio-economic position. The spread of the T2DM epidemic to these groups will have substantial implications for Thailand's health care system and economic development.

Additional interventions are needed to address the risk factors evaluated in this research. Interventions should include the promotion of the reduction in smoking and alcohol consumption (particularly in men) and SSB consumption (particularly in women). This can be done through policy (e.g. taxation), advertising restrictions and/or through public education programs. Furthermore, lower BMI-cut points could be used to define T2DM risk in Thai adults. Public health action targeting the identified risks from this work is paramount for controlling diabetes in Thailand

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10

APPENDICES

10 Appendices

Chapter 10 contains the seven appendices that support this thesis.

10.1 Appendix A – Validation study documents

Participant Information Sheet (English)

Dear Thai Cohort Study member,

My name is Keren Papier and I am a PhD student at the National Centre for Epidemiology and Population Health in the Research school of Population Health at the Australian National University. I am a qualified public health nutritionist who is interested in researching how diet affects health, particularly diabetes. You have been sent this information sheet to tell you about a small study that I am conducting with members of the Thai Cohort Study team to try to better understand what is causing the rise in diabetes cases in Thailand.

Project Title: Risk factors for type 2 diabetes mellitus in transitional Thailand

Diabetes is becoming a big problem in Thailand and we want to use information from the Thai Cohort Study (TCS) to understand this problem better. To help us with this, we want to talk to people from the Cohort who indicated in their earlier questionnaires that they had diabetes, as well as people who said that they did not have diabetes. We have selected you from among the TCS cohort members and will try to contact you by telephone over the next few weeks to ask if you would participate in a short 10 minute phone interview about your health. The information that you provide in your phone interview will help us to investigate diabetes among adults involved in the Thai Cohort Study

If you take part, the information that you provide during the interview will be linked with your previous TCS survey data using your unique TCS study number. Our plan is to publish our results in publicly available journals. None of your individual information will be published - all results will be based on the group as a whole. The results will then be available on our Thai Health-Risk Transition website and you will be able to access them there if you are interested.

Your participation in this interview is completely voluntary and you may withdraw from the study at any time prior to the preparation of the publication of the study results without any repercussions and it will not affect your participation in the larger Thai Cohort Study at all. If withdraw from this new study any information you have told us in the interview will be destroyed and not used by the research team.

What does participation in the research request of you? Your participation in this study will require for you to take part in a 10 minute phone interview with a medical practitioner who works with the Thai Cohort Study team. During the phone interview you will be asked to answer some general questions about whether or not you have been diagnosed or had tests for diabetes. Your interview will help us understand how accurately we are recording information about diabetes in using our mailed-out questionnaires.

Location and Duration: The medical practitioner will call you from a private room at STOU and arrange with you to conduct the interview at a convenient time.

Risks: The medical practitioner will be asking some questions about diabetes. Sometimes people can feel uncomfortable speaking about their health but we assure you that you do not have to answer any questions that make you feel uncomfortable. After the interview the information that you give us will be entered into a database identifiable only by your study ID number.

Confidentiality: We assure you that all of your information will remain confidential as far as allowed by law. Your name and other details will never be released. All your personal details will be kept separate from your interview responses. Your personal details will be encrypted and stored in a special database with the encryption code only available to the data manager STOU in Thailand where the research is based. The linkage of your interview information and information that you have previously provided in the written questionnaires will be carried out by the researcher using only your personal TCS ID number - not your name or other details. Other researchers on the study team will be consulted about the analysis of the linked data however they will not have access to your name or contact details. The medical practitioner will not be involved in the data linkage and will not have access to your previous survey data.

Data Storage:

Where: Your interview information will be stored at STOU in Thailand in a secure office on the main campus with 24-hour guards on patrol.

How long: All your interview information will be stored for at least five years following any publication of results.

Destruction of Data: At the end of the 5 year storage period the paper version of the interview information will be destroyed.

Queries and Concerns:

Contact Details for More Information: If you have any enquiries or require further information on this process you can contact Keren Papier, principle investigator of this study via email at keren.papier@anu.edu.au or using telephone number +61429473005. Alternatively you may also contact

Dr Sam-ang Seubsman, supervisor and Principal Investigator of the Thai Health-Risk Transition study via email Sam-ang.Seubsman@anu.edu.au. Otherwise, further details regarding the survey itself can also be accessed from our website http://nceph.anu.edu.au/research/projects/thai-cohort-study. Our office is located in the Trisorn Building Room 10, STOU and our telephone number is +66 2504 7780.

Overseas Contacts (if relevant): For further enquiries or should you feel any distress following the interview please also feel free to contact the Research and Development Institute of STOU which is located at Bangpood, Pakket Nonthaburi 11120: Thailand and their telephone number is +66 2 504 7590 and their fax number is +66 2504 7780.

Ethics Committee Clearance:

The ethical aspects of this research have been approved by the ANU Human Research Ethics Committee. If you have any concerns or complaints about how this research has been conducted, please contact:

Ethics Manager,
The ANU Human Research Ethics Committee,
The Australian National University,
Telephone: +61 2 6125 3427
Email: Human.Ethics.Officer@anu.edu.au

Participant Information Sheet (Thai)

เรียน คุณ .....

ที่อยู่ ....

เอกสารชี้แจงผู้เข้าร่วมการวิจัย

ดิฉันชื่อ Ms.Keren Papier นักศึกษาปริญญาเอกจากมหาวิทยาลัยแห่งชาติออสเตรเลีย (National Centre for Epidemiology and Population Health, Research school of Population Health) และเป็นนักโภชนาการที่กำลังดำเนินงานวิจัยเกี่ยวกับ ผลกระทบของการรับประทานอาหารต่อสุขภาพโดยเฉพาะโรคเบาหวาน เอกสารชี้แจงผู้เข้าร่วมการวิจัยฉบับนี้ เป็นเอกสารชี้แจงรายละเอียดของงานวิจัยของดิฉันที่มีกลุ่มตัวอย่างเป็นสมาชิกของโครงการวิจัยสุขภาพ มหาวิทยาลัยสุโขทัยธรรมาธิราช (Thai Cohort Study) โดยมีเป้าหมายเพื่อศึกษาและเข้าใจสาเหตุของอุบัติการณ์โรคเบาหวานประเทศไทย ภายใต้งานวิจัยชื่อ “ปัจจัยเสี่ยงต่อโรคเบาหวานชนิด 2 ของประเทศไทยในระยะเปลี่ยนผ่าน (Risk factors for type 2 diabetes mellitus in transitional Thailand)”

เพื่อความเข้าใจที่ดียิ่งขึ้นเกี่ยวกับโรคเบาหวานในกลุ่มสมาชิกโครงการวิจัยสุขภาพฯ คณะวิจัยมีความประสงค์จะขอทำการสัมภาษณ์สมาชิกที่เคยตอบแบบสอบถามที่ผ่านมาเกี่ยวกับประวัติโรคเบาหวาน ทั้งท่านที่เป็นหรือไม่เป็นเบาหวาน โดยจะมีการติดต่อถึงท่านทางโทรศัพท์ภายใน 1-2 สัปดาห์เพื่อถามความสมัครใจและให้ข้อมูลสุขภาพของท่านทางโทรศัพท์ โดยใช้เวลาประมาณ 10 นาที ข้อมูลของท่านมีประโยชน์เป็นอย่างยิ่งต่อเราในการสำรวจสาเหตุการเกิดโรคเบาหวานในวัยผู้ใหญ่ของโครงการวิจัยสุขภาพฯ

<u>หากท่านตกลงร่วมในโครงการวิจัย</u> ข้อมูลของท่านที่ให้ทางโทรศัพท์จะมีการเชื่อมต่อกับข้อมูลที่ท่านเคยให้ไว้กับโครงการวิจัยสุขภาพฯก่อนหน้านี้ ซึ่งผลวิจัยที่ได้จะถูกตีพิมพ์ในวารสารวิชาการโดยไม่มีการเปิดเผยข้อมูลส่วนตัวของท่าน นอกจากนี้ผลวิจัยจะปรากฏอยู่บนเว็บไซต์ของโครงการวิจัยฯ ซึ่งท่านสามารถอ่านได้หากมีความสนใจ ทั้งนี้ การให้ความร่วมมือในการสัมภาษณ์ของท่านจะเป็นไปด้วยความสมัครใจและท่านสามารถถอนตัวออกจากงานวิจัยนี้ได้ทุกเมื่อโดยปราศจากเงื่อนไขหรือผลกระทบใดๆต่อโครงการหลัก (โครงการวิจัยสุขภาพฯ) หากทีมวิจัยได้รับแจ้งการขอถอนตัวในงานวิจัยนี้ข้อมูลจากการสัมภาษณ์ของท่านจะไม่ถูกนำมารวมใช้ในการศึกษา

<u>สิ่งที่งานวิจัยประสงค์จากท่าน</u> ท่านจะถูกสัมภาษณ์ 10 นาทีโดยแพทย์วิชาชีพซึ่งทำงานร่วมกับโครงการวิจัยสุขภาพฯ ในการสัมภาษณ์จะขอให้ท่านตอบคำถามทั่วไปที่เกี่ยวข้องกับโรคเบาหวาน ท่านเคยได้รับการวินิจฉัยหรือทดสอบโรคเบาหวานหรือไม่ ข้อมูลที่ท่านให้จะช่วยให้เราประเมินความถูกต้องของข้อมูลโรคเบาหวานที่เราเคยได้รับจากแบบสอบถามที่เคยถูกส่งออกไปทางไปรษณีย์ก่อนหน้านี้

<u>สถานที่และระยะเวลา</u> แพทย์วิชาชีพของเราจะโทรศัพท์หาท่านจากห้องทำงานส่วนตัวที่มหาวิทยาลัยสุโขทัยธรรมาธิราช โดยติดต่อท่านเฉพาะเวลาที่ท่านสะดวกที่จะให้การสัมภาษณ์

<u>แผนการควบคุมความเสี่ยง</u> แพทย์วิชาชีพของเราจะถามคำถามที่เกี่ยวข้องกับโรคเบาหวาน โดยท่านสามารถเลือกที่จะปฏิเสธไม่ให้ข้อมูลหากคำถามนั้นทำให้ท่านเกิดความไม่สบายใจ และหลังการสัมภาษณ์ข้อมูลของท่านจะถูกบันทึกไว้ในคลังข้อมูลงานวิจัยด้วยหมายเลขสมาชิกโครงการวิจัยเท่านั้น

<u>นโยบายการรักษาข้อมูลส่วนบุคคล</u> ข้อมูลของท่านจะถูกปิดเป็นความลับโดยไม่มีการเผยแพร่ชื่อเจ้าของข้อมูล และข้อมูลส่วนตัวจะถูกเก็บรักษาด้วยระบบรักษาความปลอดภัยระดับสูงภายในมหาวิทยาลัยสุโขทัยธรรมาธิราช การเชื่อมต่อข้อมูลจากการให้สัมภาษณ์ที่ได้จากแบบสอบถามที่ท่านเคยระบุก่อนหน้านั้น และจะใช้แค่เพียงรหัสสมาชิกโครงการวิจัยสุขภาพฯเท่านั้นไม่ใช่จากชื่อจริงหรือข้อมูลอื่นๆ

การเก็บรักษาข้อมูล

- สถานที่เก็บ ข้อมูลจากการสัมภาษณ์ของท่านจะถูกเก็บในสถานที่ปลอดภัยภายในมหาวิทยาลัยสุโขทัยธรรมาธิราช ซึ่งมีเจ้าหน้าที่รักษาความปลอดภัยดูแลตลอด 24 ชั่วโมง
- ระยะเวลาการเก็บรักษาข้อมูล หลังจากมีการตีพิมพ์ผลงานวิจัยใดๆ ข้อมูลจากการสัมภาษณ์ทั้งหมดจะยังคงถูกจัดเก็บเป็นระยะเวลาอย่างน้อย 5 ปี
- กำหนดระยะเวลาการทำลายข้อมูล เอกสารกระดาษที่มีการบันทึกข้อมูลจากการสัมภาษณ์จะถูกทำลายเมื่อสิ้นสุดระยะการจัดเก็บ 5 ปี

หากท่านมีข้อสงสัย ความข้องใจ หรือต้องการรายละเอียดเพิ่มเติม ติดต่อได้ที่

- Ms.Keren Papier (นักวิจัยหลัก) อีเมล์ keren.papier@anu.edu.au มือถือ (ประเทศออสเตรเลีย) +61 4 2947 3005 หรือ รศ.ดร.สำอาง สืบสมาน (อาจารย์ที่ปรึกษาและหัวหน้าโครงการวิจัยสุขภาพฯ) อีเมล์ Sam-ang.Seubsman@anu.edu.au หากท่านต้องการทราบรายละเอียดเพิ่มเติมเกี่ยวกับการสำรวจ ท่านสามารถอ่านเพิ่มเติมได้ที่ http://nceph.anu.edu.au/research/projects/thai-cohort-study โดยมีสำนักงานตั้งอยู่ที่ อาคารตรีศร ห้อง 10 มหาวิทยาลัยสุโขทัยธรรมาธิราช โทรศัพท์ 0 2504 7780
- สถาบันวิจัยและพัฒนา มหาวิทยาลัยสุโขทัยธรรมาธิราช ถนนแจ้งวัฒนะ ตำบลบางพูด อำเภอปากเกร็ด จังหวัดนนทบุรี รหัสไปรษณีย์ 11120 โทรศัพท์ 0 2504 7590 โทรสาร 0 2504 7780

หากท่านมีข้อกังวล หรือประสงค์ให้ข้อเสนอแนะเพิ่มเติมที่เกี่ยวข้องกับการรับรองจริยธรรมงานวิจัย ติดต่อได้ที่

- คณะกรรมการจริยธรรมการวิจัย Ethics Manager, The ANU Human Research Ethics Committee, The Australian National University โทรศัพท์ +61 2 6125 3427 อีเมล์ Human.Ethics.Officer@anu.edu.au

ORAL CONSENT SCRIPT for Participants

Risk factors of type 2 diabetes mellitus in transitional Thailand

I have read to you the Information Sheet about the research project. Was this information clear? Do you have any questions about the project?

Do you agree to participate in this project? (Yes/No)

When I prepare the research outputs, I can attribute information to you in three ways: full name, pseudonym, or I can use NO attribution and hold your information confidentially.

Would you prefer that your information be treated as completely confidential? (Yes/No)

May we start the interview now?

Interview protocol for Participants with self-report diabetes

Dear …….. *TCS id*_____

My name is Prasutr Thawornchaisit and I am a medical doctor at (hospital name)

I am from STOU and the Thai Cohort Study project and I would like to ask you some questions about health. Because diabetes is becoming so important in Thailand, we need to study in more detail. So I hope that you won't mind taking part in a quick phone interview?

In our records we have you recorded as having diabetes in 2009 and/or in 2013. We were wondering if we got that right so I wanted to ask you

1. Has a doctor/ or nurse ever told you that you definitely have diabetes?	Yes☐...go to Q1A. No☐...go to Q4A.
1A. What year did a doctor/ or nurse diagnose you with diabetes?	
1B. Have you been told since then that you no longer have diabetes?	Yes☐…continue Q1 No☐...go to Q2A
1B.1 If yes then why was that? -please explain here	
1C. Were you taking steroid medication at the time of your diagnosis?	Yes☐ No☐
1D. Did you have a serious illness or surgery at the time of your diagnosis?	Yes☐ No☐
Q1E is about gestational diabetes-Skip if male and continue to Q2	
1E. Gestational diabetes	
1E.1 Were you pregnant during the diagnosis of diabetes in 2009	Yes☐...go to 1E.2 No☐
1E.2 Did the problem go away soon after your baby was born?	Yes☐ No☐
2. *We would like to know more about how you originally came to be*	

diagnosed with diabetes	
2A. How did the doctor/ or nurse diagnose you with diabetes?	
a. Using a blood test *(sometimes you would drink a sweet/ sugary drink before the blood test)*	Yes☐ No☐
b. Using a urine test	Yes☐ No☐
3. *We would like to know more about your treatment*	
3A. What treatment/s are you on for diabetes?	
1. Insulin (injected)	Yes☐ No☐
2. Tablets for diabetes	Yes☐ No☐
3. Only diet and exercise	Yes☐ No☐
4. No treatment-please explain here	Yes☐… explain No☐
4. *In order to help us improve our questionnaire and to see if we correctly interpreted your response, would you mind if I read back the question that we asked in the 2009 questionnaire and see what you think?* - please read them back the question from the 2009 questionnaire	
4A.Please indicate here if clear what the issue was *e.g. question interpreted to mean 'tested' for diabetes, question unclear; misunderstanding; clerical or scanning error.*	
5. *You have been very helpful today and we really appreciate your time*	
5A. Would we be able to contact you again if we have any further question?	Yes☐ No☐

Thank you very much for all of your time and help today!

Interview protocol for Participants with no self-report diabetes

Dear…… *TCS id*_____

My name is Prasutr Thawornchaisit and I am a medical doctor at (hospital name)

I am from STOU and the Thai Cohort Study project and I would like to ask you some questions about health. Because diabetes is becoming so important in Thailand, we need to study in more detail. So I hope that you won't mind taking part in a quick phone interview?

In our records we have you recorded as Not having diabetes in 2013. We were wondering if we got that right so I wanted to ask you

1. Can you confirm that you did not have diabetes in 2013?	Yes☐...go to Q5 No/ unsure☐...go to Q2
2. *In order to help us improve our questionnaire and to see if we correctly interpreted your response, would you mind if I read back the question that we asked in the 2013 questionnaire and see what you think?* - please read them back the question from the 2013 questionnaire	
2A. Please indicate here if clear what the issue was *e.g. question interpreted to mean 'tested' for diabetes, question unclear; misunderstanding; clerical or scanning error.*	
3. *We would like to know more about how you originally came to be diagnosed with diabetes*	
3A. How did the doctor/ or nurse diagnose you with diabetes?	
a. Using a blood test *(sometimes you would drink a sweet/sugary drink before the blood test)*	Yes☐ No☐
b. Using a urine test	Yes☐ No☐
4. *We would like to know more about your treatment*	
4A. What treatment/s are you on for diabetes?	
1. Insulin (injected)	Yes☐ No☐
2. Tablets for diabetes	Yes☐ No☐
3. Only diet and exercise	Yes☐ No☐
4. No treatment-please explain here	Yes☐… please explain No☐
5. *You have been very helpful today and we really appreciate your time*	
5A. Would we be able to contact you again if we have any further question?	Yes☐ No☐

Thank you very much for all of your time and help today!

10.2 Appendix B – Dietary survey documents

Participant Information Sheet (English)

Dear Thai Cohort Study member,

Researcher:

My name is Keren Papier and I am a PhD student at the National Centre for Epidemiology and Population Health at the Australian National University where I am working with the Thai Cohort Study (TCS) team. I am a qualified public health nutritionist who is interested in researching the diets and health of populations. I am writing to invite you to take part in a short survey and this information sheet will tell you what the study is about.

Project Title: Patterns of dietary behaviour amongst Thai Cohort Study participants

General Outline of the Project:

Description and Methodology: Diabetes is becoming a big problem in Thailand. One possible cause of rising rates of diabetes in Thailand may be changes in diets in the population over time. To enable us to investigate whether this might be the case, we want to know more about the different types of foods that people eat and what characteristics of people (age, sex, where they live, particular foods they eat) are associated with particular diet patterns.

Participants: We are inviting almost 1200 people who have previously taken part in all three surveys of the Thai Cohort Study to complete this survey and your name has been randomly selected from amongst the participants

Use of Data and Feedback: If you take part, the information that you provide in this questionnaire will be linked with information you have provided in your previous TCS surveys using your unique TCS study number. The linking of the information that you provide in this survey will allow us to explore the association between your food shopping patterns, your overall dietary pattern and your consumption of individual food items that have previously been associated with certain health risks. Establishing whether particular food acquisition and consumption patterns may be related to certain dietary patterns will help us to better understand the relationship between particular foods and diabetes risk among Thai Cohort Study participants.

We plan to publish our results in publicly available journals and to share these results with the Ministry of Public Health. None of your individual information will be published - all results will be based on the group as a whole. The results will then be available on our Thai Health-Risk Transition website and you will be able to access them there if you are interested.

Participant Involvement:

Voluntary Participation & Withdrawal: Your participation in this study is completely voluntary and you may withdraw from the study at any time prior to the preparation of the publication of the study results without any repercussions and it will not affect your participation in the larger Thai Cohort Study at all. If you withdraw from this new study any information you have provided in the survey will be destroyed and not used by the research team.

What does participation in the research request of you? If you take part we will ask you to fill in the attached questionnaire and return it in the provided post-paid envelope. The questionnaire asks you about your food shopping habits and about how frequently you eat various foods.

Duration: It should take you around 15 minutes to complete.

Confidentiality:

Confidentiality: The information that you give us will be entered into a secure database identifiable only by your study ID number and will remain confidential as far as allowed by law. All your personal details will be kept separate from your questionnaire responses. Your personal details are encrypted and stored in a special database with the encryption code only available to the data manager STOU in Thailand where the research is based. The linkage of your new questionnaire information and information that you have previously provided in the written questionnaires will be carried out by the researcher using only your personal TCS ID number - not your name or other details. Other members of the study team involved in this research will not have access to your name or contact details.

Data Storage:

Where: Your questionnaire information will be stored at STOU in Thailand in a secure office on the main campus with 24-hour guards on patrol.

How long: All your questionnaire information will be stored for at least five years following any publication of results. At the end of the storage period the paper version of the questionnaire information will be destroyed.

Queries and Concerns:

Contact Details for More Information: If you have any questions or require further information on this research you can contact **Keren Papier**, principal investigator of this study via email at keren.papier@anu.edu.au or using telephone number +61429473005. Alternatively you may also contact **Dr Sam-ang Seubsman**, supervisor and Principal Investigator of the Thai Health-Risk Transition study via email Sam-ang.Seubsman@anu.edu.au. Otherwise, further details regarding the survey itself can also be accessed from our website http://nceph.anu.edu.au/research/projects/thai-cohort-study. Our office is located in the Trisorn Building Room 10, STOU and our telephone number is +66 2504 7780.

Ethics Committee Clearance:

The ethical aspects of this research have been approved by the ANU Human Research Ethics Committee. If you have any concerns or complaints about how this research has been conducted, please contact:

Ethics Manager,
The ANU Human Research Ethics Committee,
The Australian National University,
Telephone: +61 2 6125 3427
Email: Human.Ethics.Officer@anu.edu.au

Dietary Survey – English

Questionnaire

Patterns of dietary behaviour amongst Thai Cohort Study Participants

TCSID | | | | | | | |

Dear Thai Cohort Study members,

Acknowledging all your much valued participation in Thai Health Research Project in replying to questionnaires from 2005 to 2013, Keren Papier, a nutritionist and Ph.D. candidate from Australian National University, is interested in researching further about the diets of cohort members. We therefore kindly ask you to answer this questionnaire attached herewith.

Your participation is voluntary. If you wish to withdraw at any time please inform us. The project follows strict ethical standards and all of your personal information will be held in the strictest confidence. Your name and address will be kept separately from your other data and will used only for future contact.

If you are the person whose name appears on the document above and you are willing to participate in this research, please sign your name in this form below. When you have completed the questionnaire, please return it in the envelope included here. You do not need to attach a stamp.

(Name) .....Date ..... / ..... / .....

(Mr/Mrs/Miss ....)

Mobile phone..... Home phone..... Work phone.....

If you have any doubts or concerns or need information on the project, please contact us on 02-504-7780 during business hours. Thanks and regards.

Keren Papier

Nutritionist and Ph.D. candidate in the Thai Cohort Study

A collaboration between Sukhothai Thammathirat Open University and Australian National University

This page will be separated and treated as confidential

Explanation: Please use a blue or black pen to place X mark in selected box ❑, which will look like this ☒
If somehow a question appears unclear, please select answers that suit best. Your answer will still be very valuable for research.

Food source and food consumption

1. How often do you shop for ingredients for food to be prepared at home at each of the food sources listed below? *(Please place a ✕ in the one ❑ which fits best for each type of food store).*

Food source	Never/ less than once a month	1-3 times a month	1-2 times a week	Everyday/ almost everyday
Fresh market	❑	❑	❑	❑
Mobile food vendor/ stall	❑	❑	❑	❑
Mom and pop store	❑	❑	❑	❑
Convenience store	❑	❑	❑	❑
Supermarket	❑	❑	❑	❑

2. **How often is your evening meal obtained from the following food sources?**
(Please place a ✕ in the one ❑ which fits best for each type of food store)

Evening meal food source	Never/ < than once a month	1-3 times a month	1-2 times a week	Everyday/ almost everyday
Food prepared in your home	❑	❑	❑	❑
Street vendor / Market stall / night market	❑	❑	❑	❑
Thai restaurant	❑	❑	❑	❑
Other restaurant eg western, Korean	❑	❑	❑	❑
Home delivery	❑	❑	❑	❑
Food court in shopping mall	❑	❑	❑	❑
Fast food restaurant eg pizza KFC	❑	❑	❑	❑

3. Generally in a week, how many days per week do you eat vegetables? ❑ **days per week** **(please put number)**

4. Generally in a week, how many days per week do you eat fresh fruits? ❑ **days per week** **(please put number)**

5. **Do you normally eat 3 meals per day?** Yes ❑ ⟶ go to question 7 No ❑

6. **What is the most common meal that you don't eat?** Breakfast ❑ Lunch ❑ dinner ❑

7. **On a Saturday or Sunday how many meals (breakfast lunch dinner) do you eat out of home?** *out of home food means foods not cooked from home*

Number of meals per day ❑ 0 meal⟶ go to question 10 ❑ 1 meal ❑ 2 meals ❑ 3 meals

8. **On a Saturday or Sunday what is the most common type of out of home food you eat?**

❑ ready cooked meal ❑ made-to-order meal ❑ processed food in a bag/can
❑ agreed upon time-place-type-amount-cooked meal delivery service paid on monthly basis
❑ frozen ready meal in food storage which is reheated before eating

9. On a Saturday or Sunday, which food source was the meal that you eat most often bought from ?

❑ automobile/boat vendor/sidewalk/street vendor

❑ market/market that opens only certain day/days of the week (permanent spot)

❑ made-to-order food shop/restaurant/general food shop (permanent built)

❑ convenience store ❑ fast food shop ❑ supermarket in shopping mall

10.On average, how often do you eat the following types of food *(please cross the one box which fits best for each food type)*

	Never or less than monthly	1-3 times/ month	1-2 times/ week	3-6 times/ week	Daily or more
Food or dessert with coconut milk	❑	❑	❑	❑	❑
Deep fried food	❑	❑	❑	❑	❑
Instant foods eg instant noodles	❑	❑	❑	❑	❑
Fermented/salted raw food eg crab, fish	❑	❑	❑	❑	❑
Fermented fruit/vegetable	❑	❑	❑	❑	❑
White rice or white sticky rice	❑	❑	❑	❑	❑
Brown or combined brown and white rice	❑	❑	❑	❑	❑
Fish and fish products	❑	❑	❑	❑	❑
Soft drink (eg 7-Up, coke, pepsi)	❑	❑	❑	❑	❑
Other sweetened drinks (eg iced tea or coffee, sweetened herb drinks)	❑	❑	❑	❑	❑
Milk-fresh, carton or powder	❑	❑	❑	❑	❑
Vitamins or food supplements	❑	❑	❑	❑	❑
Fast food Western style eg hamburger pizza	❑	❑	❑	❑	❑
Western bakery products eg cake, cookies	❑	❑	❑	❑	❑

11. How many serves of vegetables do you eat per day? [ ][ ] serves/day eg, *if you eat 3 serves please put* [0][3]

(1 serve of vegetables =1/2 cup of cooked vegetables or 1 cup of raw vegetables)

12. How many serves of fruit do you eat per day? [ ][ ] serves/day eg, *if you eat 5 serves please put* [0][5]

(1 serve of fruit = 1 banana or 1 slice of papaya cut into 5-6 bite-size pieces)

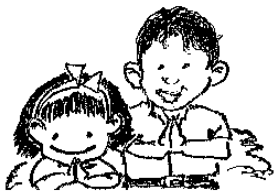
The following questions may look similar to other questions, however, your every answer is valuable for analysis of this study.


13.Food frequency

On average, how often do you normally eat the following types of food?	Don't eat at all	Less than once per month	1-3 times per month	1-3 times per week	4-6 times per week	once a day	More than once per day
1.Beef, pork, chicken, duck meat without skin	❑	❑	❑	❑	❑	❑	❑
2.Beef, pork, chicken, duck meat with skin	❑	❑	❑	❑	❑	❑	❑
3.Meat products which have been processed(group 1) eg sausage,	❑	❑	❑	❑	❑	❑	❑
4.Meat products which have been processed (group 2) eg dried	❑	❑	❑	❑	❑	❑	❑
5.Fish including fresh and salt water fish	❑	❑	❑	❑	❑	❑	❑
6.Shrimp, shellfish, crab, squid	❑	❑	❑	❑	❑	❑	❑
7.Liver (pig, duck or chicken)	❑	❑	❑	❑	❑	❑	❑
8.Whole eggs	❑	❑	❑	❑	❑	❑	❑
9.Legumes and their products (but not drinks) – eg mung beans, soy beans, tofu, vegetarian protein	❑	❑	❑	❑	❑	❑	❑
10.White rice	❑	❑	❑	❑	❑	❑	❑
11.Brown rice	❑	❑	❑	❑	❑	❑	❑
12.Sticky rice	❑	❑	❑	❑	❑	❑	❑
13.Rice noodles	❑	❑	❑	❑	❑	❑	❑
14.Instant noodles	❑	❑	❑	❑	❑	❑	❑
15.White bread	❑	❑	❑	❑	❑	❑	❑
16.Wholemeal bread	❑	❑	❑	❑	❑	❑	❑
17.Deep fried foods eg deep fried pork or chicken, deep fried bananas	❑	❑	❑	❑	❑	❑	❑
18.Western style fast food eg pizza, hamburger	❑	❑	❑	❑	❑	❑	❑
19.Curry style dishes with oil or coconut milk eg red curry, Tom Kha,	❑	❑	❑	❑	❑	❑	❑
20.Fermented foods eg fermented salted fish (plaa raa), fermented beans	❑	❑	❑	❑	❑	❑	❑
21.Chili dipping sauces (nam prik)	❑	❑	❑	❑	❑	❑	❑
22.Sweet fruits eg grapes, longan, lytchee, mangoarcane, banana, ripe papaya, watermelon, pineapple	❑	❑	❑	❑	❑	❑	❑

13. Food frequency (continued)

	Don't eat at all	Less than once per month	1-3 times per month	1-3 times per week	4-6 times per week	once a day	More than once per day
23.Not very sweet fruits eg guava, rose apple, green	❑	❑	❑	❑	❑	❑	❑
24.fruit paste, processed fruit	❑	❑	❑	❑	❑	❑	❑
25.candied fruit	❑	❑	❑	❑	❑	❑	❑
26.Fermented/pickled fruit or vegetables	❑	❑	❑	❑	❑	❑	❑
27.Canned fruit	❑	❑	❑	❑	❑	❑	❑
28.Dried fruit	❑	❑	❑	❑	❑	❑	❑
29.Fresh milk, plain (unflavoured) yoghurt	❑	❑	❑	❑	❑	❑	❑
30.Flavoured/sweetened milk or yoghurt	❑	❑	❑	❑	❑	❑	❑
31.Drinking yoghurt	❑	❑	❑	❑	❑	❑	❑
32.Skim milk	❑	❑	❑	❑	❑	❑	❑
33.Soy milk	❑	❑	❑	❑	❑	❑	❑
34.Soft drink or other sweet drinks	❑	❑	❑	❑	❑	❑	❑
35.Fruit or vegetable juice	❑	❑	❑	❑	❑	❑	❑
36.Energy drinks eg Red bull	❑	❑	❑	❑	❑	❑	❑
37.Sport drinks (egs are Thai brands but like	❑	❑	❑	❑	❑	❑	❑
38.Tea or coffee	❑	❑	❑	❑	❑	❑	❑
39.Baked goods containing butter or margarine eg	❑	❑	❑	❑	❑	❑	❑
40.Dessert made with egg yolk	❑	❑	❑	❑	❑	❑	❑
41.Desserts containing sweet syrup	❑	❑	❑	❑	❑	❑	❑
42.Desserts with coconut milk	❑	❑	❑	❑	❑	❑	❑
43.Snack foods eg potato chips	❑	❑	❑	❑	❑	❑	❑
44.Bamboo shoots	❑	❑	❑	❑	❑	❑	❑



Dietary survey – Thai

แบบสอบถาม

แบบแผนการบริโภคอาหารของสมาชิกโครงการวิจัยสุขภาพ

address

รหัสสมาชิก TCSID ☐☐☐☐☐

เรียน สมาชิกโครงการวิจัยสุขภาพที่รักทุกท่าน

ตามที่ ท่านได้ให้ความร่วมมืออย่างดียิ่งในการตอบแบบสอบถามของโครงการวิจัยสุขภาพจากการสำรวจเมื่อพ.ศ. 2548 ถึง พ.ศ. 2556 นั้น

ในการนี้ คาเรน ปาเปียร์ (Keren Papier) เป็นนักโภชนาการและกำลังศึกษาปริญญาเอก ณ มหาวิทยาลัยแห่งชาติออสเตรเลีย มีความสนใจที่จะศึกษาเรื่องอาหารของสมาชิกโครงการวิจัยสุขภาพ จึงใคร่ขอความอนุเคราะห์จากท่านตอบแบบสอบถามที่แนบมาพร้อมนี้

การให้ความร่วมมือของท่านในครั้งนี้ถือเป็นความสมัครใจและไม่มีผลกระทบต่อท่าน หากท่านไม่มีความประสงค์จะเป็นสมาชิกของโครงการฯ ท่านสามารถแจ้งให้โครงการทราบได้ทุกเมื่อ และโครงการฯจะยึดแนวทางจริยธรรมของการวิจัยอย่างเคร่งครัด ข้อมูลส่วนบุคคลจะจัดเก็บเป็นความลับและใช้เพื่อการติดต่อท่านในอนาคตเท่านั้น

หากท่านคือบุคคลที่ปรากฏชื่อตามเอกสารด้านบนนี้ และยินดีให้ความร่วมมือในการวิจัย โปรดลงชื่อในช่องว่างข้างล่างและตอบแบบสอบถามพร้อมส่งกลับมาในซองที่แนบ โดยไม่ต้องติดแสตมป์

sign (ลงชื่อ) ..... วันที่ ..... / ..... / ..... sdate

nsname (นาย/นาง/นางสาว .....)

หมายเลขโทรศัพท์มือถือ..... mtel โทรศัพท์บ้าน..... htel โทรศัพท์ที่ทำงาน..... wtel

หากท่านมีข้อสงสัย สอบถามรายละเอียดเพิ่มเติมได้ที่หมายเลข โทรศัพท์ 02-504-7780 ในเวลาราชการและขอขอบคุณมา ณ โอกาสนี้

(คาเรน ปาเปียร์)

นักโภชนาการและนักศึกษาปริญญาเอกในโครงการวิจัยสุขภาพ
โครงการความร่วมมือระหว่างมหาวิทยาลัยสุโขทัยธรรมาธิราช
และมหาวิทยาลัยแห่งชาติออสเตรเลีย

หน้านี้จะได้รับจัดเก็บเป็นความลับ
แยกออกจากส่วนอื่น

แต่หากยังมีคำถามที่ไม่ชัดเจน เราขอให้ท่านตอบให้ใกล้ความจริงที่สุด คำตอบของท่านจะยังเป็นประโยชน์ในการวิจัยเป็นอย่างมาก

แหล่งอาหารและการบริโภคอาหาร

1.ท่านซื้อวัตถุดิบเพื่อปรุงอาหารที่บ้านจากแหล่งต่อไปนี้บ่อยแค่ไหน

(โปรดใส่เครื่องหมาย ✕ ลงในช่องความถี่ ❑ เพียงช่องเดียวที่ตรงกับท่านมากที่สุด ต่อแต่ละประเภทแหล่งซื้ออาหาร)

แหล่งซื้ออาหาร		ไม่เคย/น้อยกว่าเดือนละครั้ง	1-3 ครั้งต่อเดือน	1-2 ครั้งต่อสัปดาห์	ทุกวัน/เกือบทุกวัน
ตลาดสด	v1n1	0	1	2	3
รถเร่/ รถเข็น	v1n2	0	1	2	3
ร้านขายของชำ	v1n3	0	1	2	3
ร้านสะดวกซื้อ	v1n4	0	1	2	3
ซูเปอร์มาร์เก็ต	v1n5	0	1	2	3

2.โดยปกติ ในมื้อเย็นท่านรับประทานอาหารจากแหล่ง/สถานที่จำหน่ายอาหารต่อไปนี้บ่อยเพียงใด

(โปรดใส่เครื่องหมาย ✕ ลงในช่อง ❑ ที่ตรงความเห็นของท่านมากที่สุด)

แหล่งอาหารมื้อเย็น		ไม่เคย / น้อยกว่าเดือนละครั้ง	1 - 3 ครั้งต่อเดือน	1 - 2 ครั้งต่อสัปดาห์	ทุกวัน / เกือบทุกวัน
อาหารปรุงที่บ้าน	v2n1	0	1	2	3
รถเร่/แผงในตลาด/ตลาดโต้รุ่ง	v2n2	0	1	2	3
ร้านขายอาหารแบบไทย	v2n3	0	1	2	3
ร้านอาหารแบบตะวันตก/เกาหลี/จีน/ญี่ปุ่น/	v2n4	0	1	2	3
อาหารบริการส่งถึงบ้าน	v2n5	0	1	2	3
ฟูดคอร์ทในห้างสรรพสินค้า	v2n6	0	1	2	3
ร้านฟาสต์ฟู้ด เช่น พิซซ่า เคเอฟซี	v2n7	0	1	2	3

3.โดยทั่วไปในแต่ละสัปดาห์ ท่านกิน ผัก กี่วันต่อสัปดาห์ ❑ วันต่อสัปดาห์ v3

4.โดยทั่วไปในแต่ละสัปดาห์ ท่านกินผลไม้สดกี่วันต่อสัปดาห์ ❑ วันต่อสัปดาห์ v4

5.โดยปกติ ท่านกินอาหารครบ 3 มื้อหลักหรือไม่ 1 ใช่ → **ข้ามไปตอบข้อ 7** 0 ไม่ใช่ v5

6.โดยส่วนใหญ่ ท่านงดกินอาหารมื้อใด 1 มื้อเช้า 2 มื้อกลางวัน 3 มื้อเย็น v6

7.ในวันเสาร์หรืออาทิตย์ ท่านกินอาหารมื้อหลัก (เช้า กลางวัน เย็น) **นอกบ้านกี่มื้อ** *อาหารนอกบ้าน หมายถึง อาหารที่ไม่ได้ทำเองที่บ้าน*

จำนวนมื้อต่อวัน v7 0 0 มื้อ → **ข้ามไปตอบข้อ 10** 1 มื้อ 2 มื้อ 3 มื้อ

8.ในวันเสาร์หรืออาทิตย์ ลักษณะอาหารนอกบ้านที่ท่านกินบ่อยที่สุด คือ v8

1 อาหารปรุงสุกสำเร็จ 2 อาหารตามสั่ง 3 อาหารสำเร็จรูปบรรจุซอง/กระป๋อง
4 อาหารปิ่นโตรับเป็นรายเดือน 5 อาหารแช่แข็งสำเร็จรูปมาเก็บไว้ เมื่อกินจะนำมาอุ่น

9. ในวันเสาร์หรืออาทิตย์ แหล่งที่มาของอาหารมื้อหลักที่ท่านกินบ่อยที่สุดเป็นอาหารที่ซื้อมาจากแหล่งใด 3

v9
1 รถเร่/เรือเร่ขายอาหาร/อาหารริมบาทวิถี/อาหารริมทาง
2 ตลาด/ตลาดนัด (ร้านไม่เคลื่อนย้าย)
3 ร้านอาหารตามสั่ง/ภัตตาคาร/ร้านอาหารทั่วไป (ร้านที่มีโครงสร้างแข็งแรง)
4 ร้านสะดวกซื้อ
5 ร้านขายอาหารฟาสต์ฟู้ด
6 ซูเปอร์มาร์เก็ตในห้างสรรพสินค้า

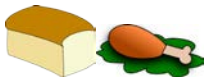
10. โดยเฉลี่ยแล้ว ท่านรับประทานอาหารต่อไปนี้ บ่อยครั้งแค่ไหน *(กาเครื่องหมาย x ลงช่องที่ตรงตามที่ท่านรับประทานจริง)*

		ไม่เคย/น้อยกว่าเดือนละครั้ง	เดือนละ 1-3 ครั้ง	สัปดาห์ละ 1-2 ครั้ง	สัปดาห์ละ 3-6 ครั้ง	วันละครั้งหรือมากกว่า
อาหาร/ขนมหวานที่ประกอบ	v10n1	0	1	2	3	4
อาหารประเภททอด	v10n2	0	1	2	3	4
อาหารกึ่งสำเร็จรูป เช่น บะหมี่	v10n3	0	1	2	3	4
อาหารหมักดอง (ดิบ) เช่น	v10n4	0	1	2	3	4
ผักผลไม้ดอง	v10n5	0	1	2	3	4
ข้าวจ้าวหรือข้าวเหนียวขัดขาว	v10n6	0	1	2	3	4
ข้าวกล้อง/หรือข้าวขาวผสมข้าว	v10n7	0	1	2	3	4
ปลา/ผลิตภัณฑ์จากปลา	v10n8	0	1	2	3	4
น้ำอัดลม เช่น โค้ก เป๊ปซี่ ฯลฯ	v10n9	0	1	2	3	4
เครื่องดื่มผสมน้ำตาล เช่น ชา กาแฟเย็น น้ำสมุนไพร	v10n10	0	1	2	3	4
นม เช่น นมสด นมกล่อง นม	v10n11	0	1	2	3	4
ผลิตภัณฑ์อาหารเสริม เช่น	v10n12	0	1	2	3	4
อาหารจานด่วนแบบตะวันตก แฮมเบอร์เกอร์ พิซซ่า	v10n13	0	1	2	3	4
ขนมแบบตะวันตก เช่น โดนัท	v10n14	0	1	2	3	4

v11
11. ท่านรับประทานผักจำนวนกี่ส่วนต่อวัน ☐☐ **ส่วนต่อวัน** เช่น ถ้ากิน 3 ส่วน ใส่ตัวเลข 0 3
(เช่น ผัก 1 ส่วน = ผักปรุงสุก ครึ่งถ้วยตวง หรือผักดิบ 1 ถ้วยตวง)

v12
12. ท่านรับประทานผลไม้จำนวนกี่ส่วนต่อวัน ☐☐ **ส่วนต่อวัน** เช่น ถ้ากิน 5 ส่วน ใส่ตัวเลข 0 5
(เช่น กล้วย 1 ลูก = 1 ส่วน หรือ มะละกอ 1 ชิ้น 5-6 คำ = 1 ส่วน)

ท่านอาจจะสังเกตว่าคำถามต่างๆคล้ายกัน อย่างไรก็ตามการตอบคำถามทุกข้อของท่าน มีประโยชน์ต่อการวิเคราะห์ข้อมูลการวิจัยในครั้งนี้ 4



13. ความถี่ในการกินอาหาร

โดยทั่วไปท่านกินอาหารในประเภทต่อไปนี้บ่อยเพียงใด		ไม่กินเลย	น้อยกว่า 1 ครั้งต่อเดือน	1-3 ครั้งต่อเดือน	1-3 ครั้งต่อสัปดาห์	4-6 ครั้งต่อสัปดาห์	1 ครั้งต่อวัน	มากกว่า 1 ครั้งต่อวัน
1. เนื้อวัว/หมูไม่ติดมัน ไก่/เป็ดไม่ติดหนัง	v13n1	0	1	2	3	4	5	6
2. เนื้อวัว/หมูติดมัน ไก่/เป็ดติดหนัง เช่น หมูสาม	v13n2	0	1	2	3	4	5	6
3. ผลิตภัณฑ์เนื้อสัตว์ที่ผ่านกระบวนการกลุ่มที่ 1 ไส้กรอก ไส้กรอกอิสาน เบคอน แฮม กุนเชียง หมูยอ แหนม	v13n3	0	1	2	3	4	5	6
4. ผลิตภัณฑ์เนื้อสัตว์ที่ผ่านกระบวนการกลุ่มที่ 2 หมูหยอง ปลาเค็ม เนื้อ/หมู/ปลาแดดเดียว	v13n4	0	1	2	3	4	5	6
5. ปลาชนิดต่างๆ เช่น ปลาน้ำจืด ปลาทะเล	v13n5	0	1	2	3	4	5	6
6. กุ้ง หอย ปู ปลาหมึก	v13n6	0	1	2	3	4	5	6
7. ตับ เลือดหมู/เป็ด/ไก่	v13n7	0	1	2	3	4	5	6
8. ไข่ทั้งฟอง หรือเฉพาะไข่แดง	v13n8	0	1	2	3	4	5	6
9. ถั่วและผลิตภัณฑ์ (ไม่รวมเครื่องดื่ม) เช่น ถั่วถั่วเหลือง ถั่วลิสง เต้าหู้ โปรตีนเกษตร	v13n9	0	1	2	3	4	5	6
10. ข้าวขาว/ข้าวขัดสี	v13n10	0	1	2	3	4	5	6
11. ข้าวกล้อง ข้าวซ้อมมือ	v13n11	0	1	2	3	4	5	6
12. ข้าวเหนียว	v13n12	0	1	2	3	4	5	6
13. ก๋วยเตี๋ยวต่างๆ ขนมจีน	v13n13	0	1	2	3	4	5	6
14. บะหมี่กึ่งสำเร็จรูป เช่น มาม่า ยำยำ ไวไว	v13n14	0	1	2	3	4	5	6
15. ขนมปังขาว	v13n15	0	1	2	3	4	5	6
16. ขนมปังโฮลวีท (ขนมปังธัญพืช)	v13n16	0	1	2	3	4	5	6
17. อาหารทอด เช่น หมู/ไก่ทอด ทอดมัน กล้วย ลูกชิ้นทอด แก็บหมู ฯลฯ	v13n17	0	1	2	3	4	5	6
18. อาหารจานด่วนตะวันตก เช่น พิซซ่า แฮมเบอ	v13n18	0	1	2	3	4	5	6
19. อาหารคาวประเภทแกงที่มีกะทิ/น้ำมัน เช่น แกงอ่อม ขนมจีนน้ำเงี้ยว	v13n19	0	1	2	3	4	5	6
20. ปลาร้า ปลาเจ่า น้ำบูดู ถั่วเน่า	v13n20	0	1	2	3	4	5	6
21. น้ำพริก เช่น น้ำพริกกะปิ น้ำพริกหนุ่ม น้ำพริกปลาป่น น้ำพริกปลาร้า น้ำพริกตาแดง น้ำพริกลงเรือ	v13n21	0	1	2	3	4	5	6

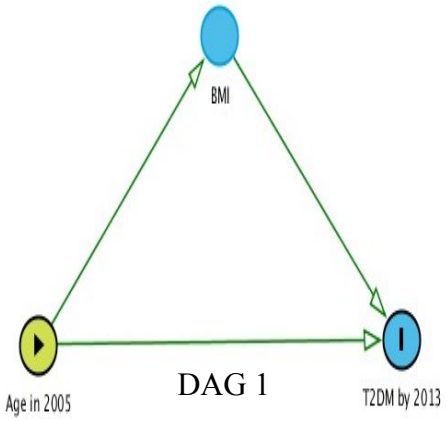
13. ความถี่ในการกินอาหาร (ต่อ) 5

โดยทั่วไปท่านกินอาหารในประเภทต่อไปนี้บ่อยเพียงใด	ไม่กินเลย	น้อยกว่า 1 ครั้งต่อเดือน	1-3 ครั้งต่อเดือน	1-3 ครั้งต่อสัปดาห์	4-6 ครั้งต่อสัปดาห์	1 ครั้งต่อวัน	มากกว่า 1 ครั้งต่อวัน
22. ผลไม้รสหวาน เช่น องุ่น ลองกอง ทุเรียน ลำไย ลิ้นจี่ มะม่วงสุก ขนุน ละมุด น้อยหน่า อ้อย กล้วย มะละกอสุก แตงโม สับปะรด ฯลฯ v13n22	0	1	2	3	4	5	6
23. ผลไม้รสไม่หวาน/หวานน้อย เช่น ฝรั่ง ชมพู่ มะม่วงดิบ แอปเปิ้ล แก้วมังกร v13n23	0	1	2	3	4	5	6
24. ผลไม้กวน ฉาบ เช่น สับปะรดกวน กล้วยฉาบ v13n24	0	1	2	3	4	5	6
25. ผลไม้เชื่อม เช่น สาเกเชื่อม กล้วยเชื่อม มะตูม v13n25	0	1	2	3	4	5	6
26. ผักและผลไม้หมักดอง เช่น ผลไม้ดอง ผักกาด v13n26	0	1	2	3	4	5	6
27. ผลไม้กระป๋อง v13n27	0	1	2	3	4	5	6
28. ผลไม้แห้ง เช่น ลูกเกด ลูกพรุน ลูกท้อ พุทรา v13n28	0	1	2	3	4	5	6
29. นมสด/โยเกิร์ตชนิดถ้วยไม่ปรุงแต่งรส v13n29	0	1	2	3	4	5	6
30. นมหวาน/นมปรุงแต่งรส/โยเกิร์ตชนิดถ้วย v13n30	0	1	2	3	4	5	6
31. โยเกิร์ตชนิดดื่ม v13n31	0	1	2	3	4	5	6
32. นมพร่องมันเนย v13n32	0	1	2	3	4	5	6
33. น้ำเต้าหู้/นมถั่วเหลือง v13n33	0	1	2	3	4	5	6
34. น้ำอัดลม/น้ำหวาน v13n34	0	1	2	3	4	5	6
35. น้ำผลไม้/น้ำผัก v13n35	0	1	2	3	4	5	6
36. เครื่องดื่มชูกำลัง เช่น กระทิงแดง ลิโพ เอ็ม v13n36	0	1	2	3	4	5	6
37. เครื่องดื่มสำหรับนักกีฬา เช่น สปอนเซอร์ v13n37	0	1	2	3	4	5	6
38. ชา กาแฟ v13n38	0	1	2	3	4	5	6
39. อาหารที่มีเนย/มาการีนและแป้ง เช่น เค้ก คุกกี้ v13n39	0	1	2	3	4	5	6
40. ขนมหวานทำจากไข่แดง เช่น ทองหยิบ v13n40	0	1	2	3	4	5	6
41. ขนมใส่น้ำเชื่อม เช่น ถั่วเขียวต้มน้ำตาล มันต้มน้ำตาล สาคูน้ำเชื่อม ลูกชิดน้ำเชื่อม v13n41	0	1	2	3	4	5	6
42. ขนมหวานที่มีกะทิ เช่น กล้วยบวดชี วุ้นกะทิ v13n42	0	1	2	3	4	5	6
43. ขนมขบเคี้ยว/ขนมกรุบกรอบบรรจุซอง v13n43	0	1	2	3	4	5	6
44. หน่อไม้ทุกประเภท v13n44	0	1	2	3	4	5	6

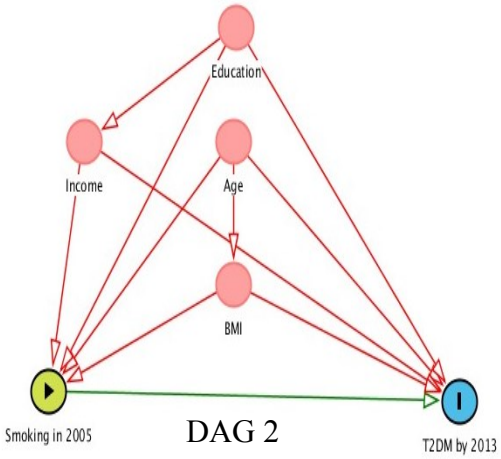
10.3 Appendix C –Directed acyclic graphs (DAGs) used in this thesis

This appendix contains the directed acyclic graphs (DAGs) I created in DAGitty v2.3 using measured variables from my dataset to describe casual relationships between various exposures of interest and type 2 diabetes; and between socio-demographic factors and dietary patterns.

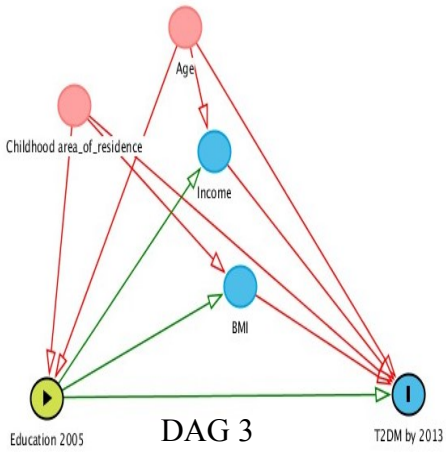
DAGs 1 to 8 are the DAGs I created to describe the casual relationships between various risk factors for T2DM incidence in 2013. These DAGs were all considered in the construction of the final analysis model in Chapter 4.



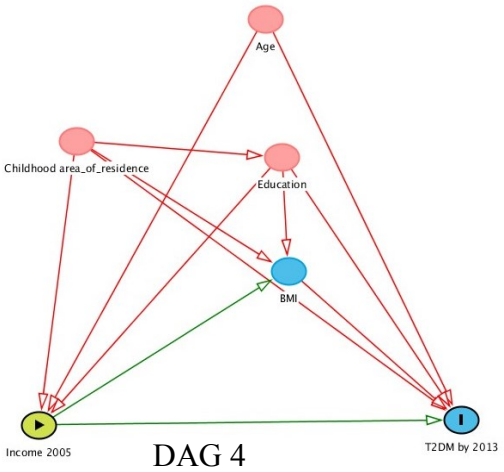
DAG 1



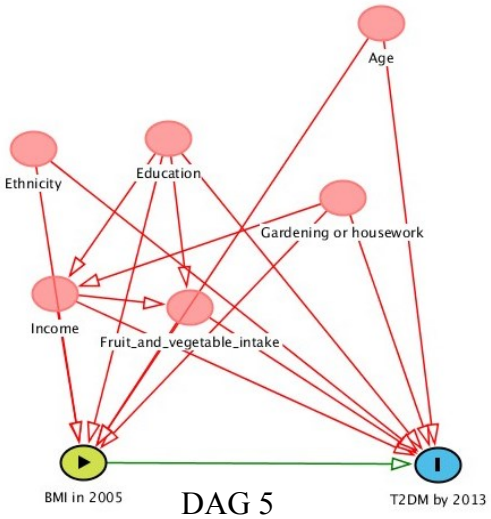
DAG 2



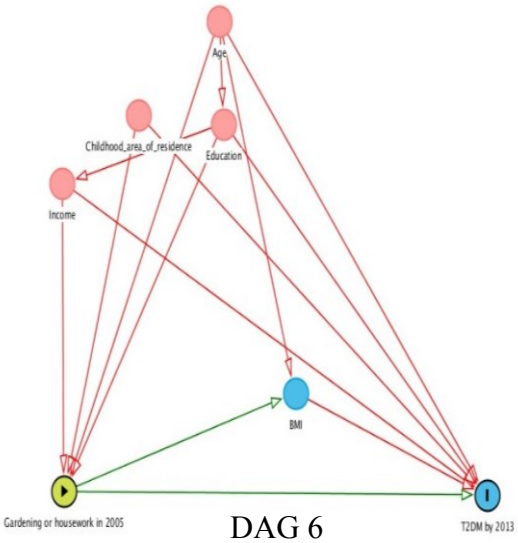
DAG 3



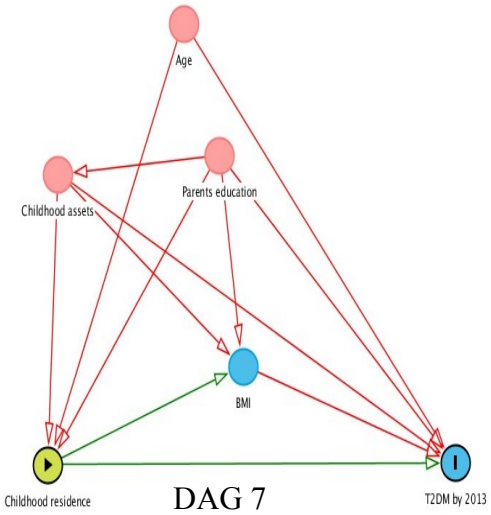
DAG 4



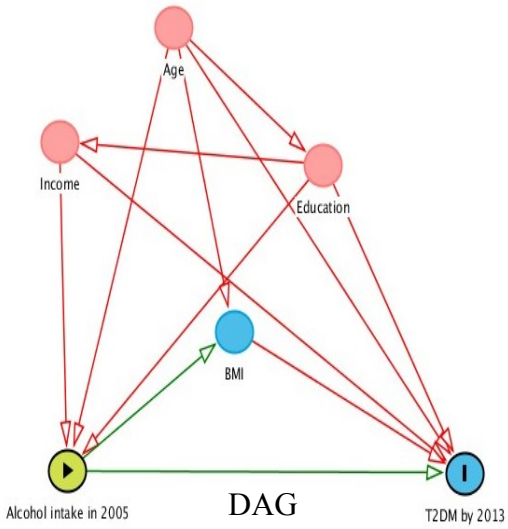
DAG 5



DAG 6

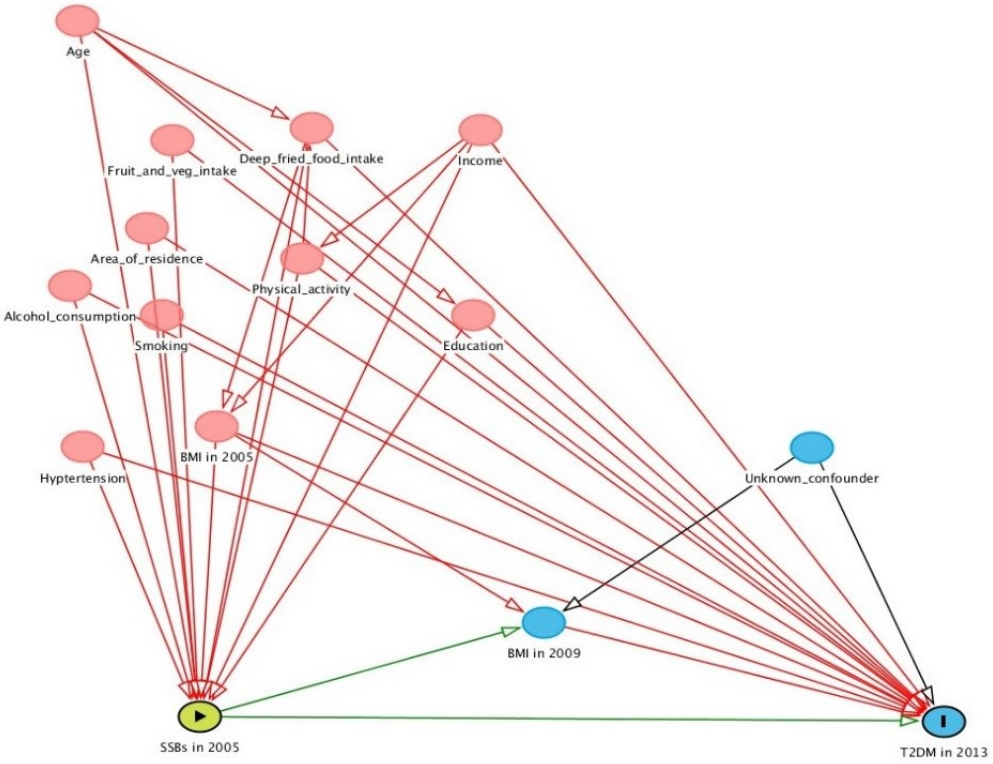


DAG 7



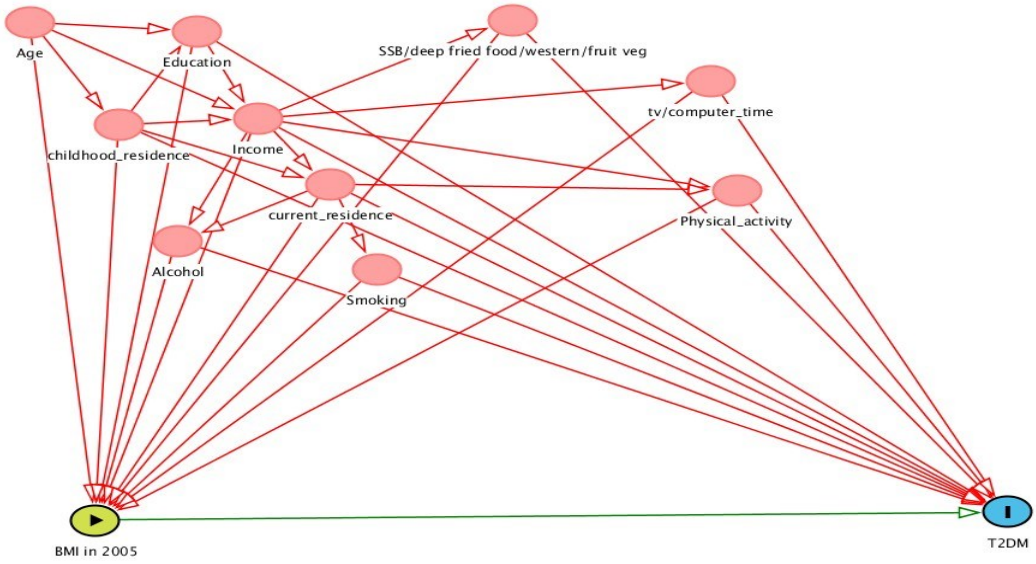
DAG

DAG 9 is the DAG I created to describe the casual relationship between sugar sweetened beverage (SSB) consumption in 2005 and T2DM incidence in 2013 (Chapter 5). Using this DAG, I was able to identify the necessary adjustments required to determine the total and direct effects of SSB intake on T2DM risk. For instance, to assess the total effect of SSB intake (2005) on T2DM risk (2013), all of the variables highlighted in pink required adjustment. Alternatively, to assess the direct effect of SSB intake (2005) on T2DM risk (2013) (using the 'traditional method') all of the variables in pink along with BMI in 2009 required adjustment.



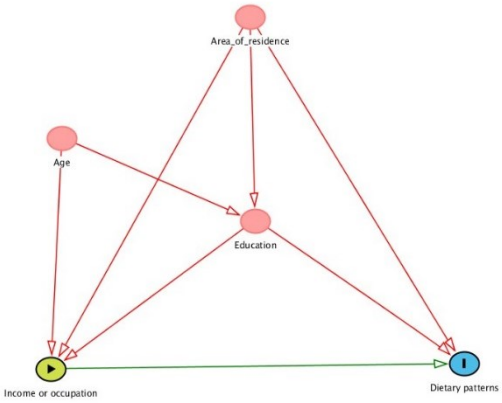
DAG 9: Directed acyclic graph displaying the minimal sufficient adjustment sets (in pink) for estimating the total effect of SSB intake in 2005 on T2DM risk in 2013

DAG 10 is the DAG I created to describe the casual relationship between BMI and T2DM incidence in 2013. This DAG was considered in the construction of the final analysis model in Chapter 6.

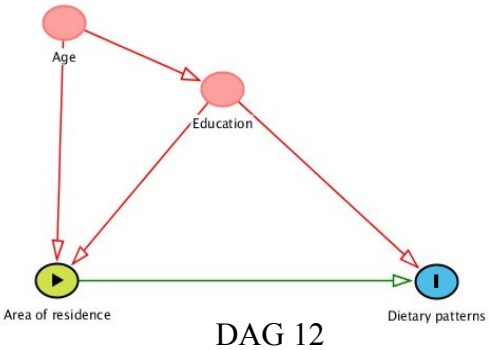


DAG 10: Directed acyclic graph displaying the minimal sufficient adjustment sets (in pink) for estimating the total effect of BMI in 2005 on T2DM risk in 2013

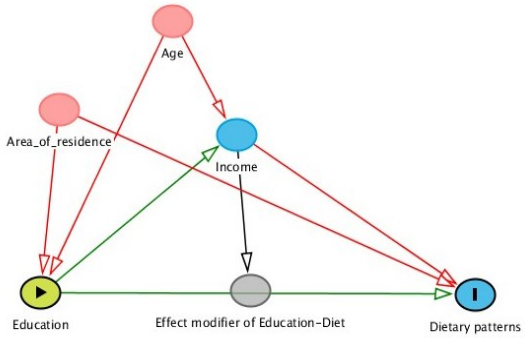
DAGs 11 to 13 are the DAGs I created to describe the casual relationships between socio-demographic factors and dietary patterns. These DAGs were all considered in the construction of the final analysis model in Chapter 7.



DAG 11



DAG 12



DAG 13

10.4 Appendix D – Peer reviewed article relevant to this thesis

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Short Communication

Relationship between 8-year weight change, body size, and health in a large cohort of adults in Thailand

Vasoontara Yiengprugsawan [a, b, *], Wimalin Rimpeekool [c], Keren Papier [d], Cathy Banwell [d], Sam-ang Seubsman [c], Adrian C. Sleigh [d]

[a] Centre for Research on Ageing, Health and Wellbeing, Research School of Population Health, Australian National University, Canberra, Australia
[b] Australian Research Council Centre of Excellence on Population Ageing Research, Canberra, Australia
[c] School of Human Ecology, Sukhothai Thammathirat Open University, Nonthaburi, Thailand
[d] National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Canberra, Australia

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ABSTRACT

Background: Overweight and obesity have been shown to be risk factors for a range of non-communicable diseases, especially cardio-metabolic conditions, worldwide. But less is known about the effects of weight change on adults' overall health and wellbeing, particularly in transitional low- and middle-income countries. This study aimed to assess the relationship between 8-year weight change and measures of self-assessed health among Thai adults.

Methods: Data were collected from Thai adults aged 25–40 years (n = 27,003) enrolled in the Thai cohort Study and surveyed in 2005, 2009, and 2013. We used self-reported weight and height measurements at baseline and 2013, as well as three standard health questions regarding overall health, energy, and emotion asked at the two time points, to investigate the effects of weight change on health.

Results: Between 2005 and 2013, 6.0% of participants lost more than 5% of their baseline weight; 38.5% were stable (<5% loss to 5% gain); 23.0% slightly gained weight (>5%–10%); 22.8% gained moderate weight (>10%–20%); and 9.4% had heavy weight gain (>20%). Moderate (>10%–20%) and heavy weight gain (>20%) were both associated with an increased risk of reporting 'poor or very poor' overall health in 2013 among participants who had a normal body mass index (BMI) (adjusted odds ratio [AOR] 1.39; 95% confidence interval [CI], 1.13–1.71 and AOR 1.44; 95% CI, 1.09–1.90, respectively), were overweight (AOR 1.53; 955 CI, 1.01–2.29 and AOR 1.82; 95% CI, 1.04–3.19, respectively) or had obesity (AOR 2.47; 95% CI, 1.74–3.51 and AOR 3.20; 95% CI, 2.00–5.16, respectively) in 2005. Weight gain of over 20% also had a negative impact on energy level among cohort members with a normal BMI in 2005 (AOR 1.36; 95% CI, 1.11–1.65) and among participants with obesity in 2005 (AOR 1.93; 95% CI, 1.38–2.71). For those who were underweight, had a normal BMI, or had obesity at baseline, weight loss of more than 5% was associated with reporting emotional problems. Excessive weight gain adversely impacted participants who were underweight or had obesity at baseline.

Conclusion: Our study found that weight change, in particular weight gain, was associated with negative health outcomes, and this effect appeared to increase at higher levels of body size. The present findings may be useful to promote weight maintenance and healthy lifestyles.

Introduction

Increasing weight, overweight, and obesity signal a growing risk of hypertension, high cholesterol, cardiovascular diseases, and other health problems throughout the world. As the global burden of disease shifts to non-communicable diseases (NCDs),[1] it becomes imperative to understand the relationships between changes in body size and health outcomes. Obesity has been known to have an impact on health and quality of life.[2,3] However, less is known about

* Corresponding author. Australian National University, Research School of Population Health, Building 54 Florey, Mills Road, Acton, 2601, Canberra, Australia.
E-mail addresses: vasoontara.yieng@anu.edu.au, vasoontara.yieng@gmail.com (V. Yiengprugsawan).

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the relationship between weight change and indicators of poorer health and quality of life, especially in low- and middle-income countries. Questions still remain about the degree of weight change associated with development of adverse health outcomes and the direction of causality over time.

In Thailand, concern has been growing about increasing obesity and diet-related health risks. Thailand has been among the leaders in Southeast Asia in its rapid urbanization and economic development over the last 3 to 4 decades, which has been accompanied by a move toward more sedentary work, car use, and an increasingly calorie-dense national diet containing more fat, sugar, and salt.[4,5] National examination health surveys conducted since 1991 (in 1991, 1997, 2004, and 2009) have shown corresponding increases in Thai body weight and in NCDs.[6,7]

This study investigates weight change over time and its relationship with three main health outcomes (self-assessed health, energy, and emotion). The study used data collected from a large sample of adult Open University students undertaking distance learning in Thailand, who reside throughout the country, are well-educated, employed, and of average income. Cohort members' longitudinal weight change over 8 years was used to predict adverse health outcomes during the 8-year follow-up.

Methods

Our initial research cohort included 87,151 distance-learning adult students enrolled at Sukhothai Thammathirat Open University who were living all over Thailand. They completed the mail-out baseline questionnaire in 2005 investigating transitional patterns of health risks and outcomes. Topics included a range of socio-demographic characteristics, family background, occupation, income, and wellbeing, and health status. The median age at baseline was 29 years, slightly more than half were females, and half resided in urban areas.[8,9] The cohort was subsequently followed up in 2009 and 2013 (capturing more than 70% at each wave). Analyses presented here were restricted to cohort members aged 25–40 years at the 2005 baseline to limit the otherwise large confounding effect of age on body mass index and health outcomes, resulting in a sample of 27,003 participants.

For our exposure of interest, body mass index (BMI) was derived from weight and height reported at each wave of data collection. We follow the International Obesity Task Force guidelines for BMI cut-offs for Asian populations: BMI 18.5 to <23 as 'normal', 23 to <25 as 'overweight at risk', and ≥25 as 'overweight and obese'[10]; these cut-offs have also been used in other studies based on our cohort.[11,12] Weight change was calculated in 2013, as a percent of 2005 baseline weight, categorized into five percentage groups:

(1) weight loss >5% (loss);
(2) weight loss or gain ≤5% (stable);
(3) weight gain >5% and ≤10% (slight gain);
(4) weight gain >10% and ≤20% (moderate gain);
(5) weight gain >20% (heavy gain)

Three variables from the standardized Medical Outcome Short Form (SF-8) instrument were used to investigate adverse outcomes for the study.[13] Subjective self-rated health has been applied in international literature to measure overall health and has been shown to be a strong predictor of mortality.[14,15] In this study, we use three main variables (self-rated health, energy level, and emotion); two of these variables had six possible responses, and one variable had five possible responses. We converted responses for each variable into a binary format as follows: the last two responses were combined into an 'adverse' outcome category for all variables, and the first three or four responses were combined into a 'non-adverse' health outcome. These adjustments permitted binary analyses. The questions were the same at the 2005 baseline and the 2013 follow-up, as follows:

- *Overall, how would you rate your health during the past 4 weeks*? (excellent, very good, good, or fair = 0; poor or very poor = 1)
- *During the past the past 4 weeks, how much energy did you have*? (very much, quite a lot, a lot, or some = 0; a little or none = 1)
- *During the past 4 weeks, how much have you been bothered by emotional problems (such as feeling anxious, depressed, or irritable)*? (Not at all, slightly, or moderately = 0; quite a lot or extremely = 1)

Initial analyses showed cohort attributes (sex, age, residence, income, and BMI) by 8-year weight change categories. We used 8-year longitudinal weight change to predict health outcomes among cohort members who did not initially report adverse health status at baseline. Analyses were stratified by 2005 BMI categories (underweight, normal, overweight, or obese) in order to investigate associations between weight change and health outcomes according to cohort members' initial body size.

Multivariate logistic analyses of the binary SF-8 health outcomes by 8-year longitudinal weight change were performed to obtain adjusted odds ratios (AORs) and 95% confidence intervals (CIs). Each set of multivariate logistic analyses only included cohort members who had not reported adverse SF-8 health outcomes at baseline (e.g., excluded 1209 for overall health, 2703 for energy level, and 3567 for emotional level). This is also one of the reasons for restricting analyses for cohort members aged 25–40 years, as older cohort members were more likely to be excluded at the baseline. Individuals with missing data for any given analyses were excluded (<5% for each variable), so totals could vary due to available information.

Ethics approval for the overall study was obtained from Sukhothai Thammathirat Open University Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocol 2009/570). Informed written consent was obtained from all participants.

Results

Among the 27,003 analyzed cohort members, 45% were males (Table 1); at baseline, 38.0% were aged 25–29 years, 30.7% were aged 30–34 years, and 31.3% were aged 35–40 years; 36.7% of cohort members reported residing in rural areas, and 41.8% resided in urban areas in both 2005 and 2013. BMI at baseline indicated that 55.4% of cohort members were normal weight, 11.6% were underweight, 16.7% were overweight, and 16.2% were obese.

Between 2005 and 2013, 6.0% of participants lost more than 5% of their baseline weight, 38.5% were stable, 23.0% had slight weight gain, 22.8% had moderate weight gain, and 9.4% had heavy weight gain (Table 1). Across the 8 years, weight maintenance (within 5% of baseline weight) was more common among males than females (42.5% vs. 35.2%) and was most common among participants aged 30–34 years (46.3%) and those in the highest income bracket (41.2%). There was little difference according to residence.

At the 8-year follow-up in 2013, 5.7% of cohort members reported 'poor or very poor' overall health, 8.9% reported 'little or none' for energy level, and 9.6% reported 'quite a lot or extremely' for emotional problems (Table 2).

The findings from the logistic regression analyses are shown in Table 2. Moderate and heavy weight gain were both associated with an increased risk of reporting 'poor or very poor' overall health in 2013 among participants who had a normal BMI (AOR 1.39; 95% CI, 1.13–1.71] and AOR 1.44; 95% CI, 1.09–1.90, respectively), were overweight (AOR 1.53; 95% CI, 1.01–2.29 and AOR 1.82; 95% CI, 1.04–3.19, respectively), or had obesity (AOR 2.47; 95% CI, 1.74–3.51

Table 1
Thai cohort member attributes at 2005 baseline and 8-year weight change between 2005 and 2013.

Cohort attributes at 2005 baseline (column %)	Eight-year weight change (row percent)				
	$\Delta \geq -5\%$	$-5\% < \Delta \leq 5\%$	$5\% < \Delta \leq 10\%$	$10\% < \Delta \leq 20\%$	$\Delta > 20\%$
Overall (n = 27,003)	6.0	38.5	23.0	22.8	9.4
Male (45.0%, n = 12,157)	6.9	42.5	22.8	20.4	7.3
Female (54.9%, n = 14,846)	5.3	35.2	23.2	24.9	11.2
Age groups					
25–29 years (38.0%)	5.1	32.3	21.7	27.2	13.5
30–34 years (30.7%)	7.3	46.3	23.7	17.4	5.1
35–40 years (31.3%)	5.8	38.5	23.9	22.9	8.7
Residence: 2005 and 2013					
Rural–rural (36.7%)	6.2	39.2	22.4	22.8	9.2
Rural–urban (12.7%)	6.3	37.9	23.5	22.7	9.4
Urban–rural (7.4%)	5.8	36.8	23.6	22.6	10.9
Urban–urban (41.8%)	5.8	38.6	23.3	22.9	9.3
Personal monthly income					
<10,000 Baht (20.1%)	7.3	38.0	20.8	22.0	11.7
10,001–30,000 Baht (64.1%)	5.5	36.0	23.4	24.6	10.3
>30,000 Baht (15.7%)	5.8	41.2	23.7	21.7	7.5
Body mass index category					
Underweight (11.6%)	1.9	35.4	23.4	27.2	11.8
Normal (55.4%)	3.8	36.9	24.4	25.2	9.4
Overweight (16.7%)	7.7	44.6	21.5	19.6	6.3
Obese (16.2%)	15.0	42.4	20.8	16.4	5.1

and AOR 3.20; 95% CI, 2.00–5.16, respectively) in 2005. Eight-year weight change was also associated with an increased risk of reporting "little or no energy" in 2013. Among participants who had a normal BMI in 2005, weight loss >5% and weight gain >10% were both associated with an increased risk of reporting 'little or no energy' in 2013. Similarly, among participants who had obesity in 2005, >20% weight gain was also associated with having reduced energy levels (AOR 1.93; 95% CI, 1.38–2.71).

Cohort members who lost >5% of their initial weight at baseline had an increased risk of reporting 'quite a lot' or 'extreme' emotional problems (AOR 1.98; 95% CI, 1.01–1.62 among cohort members who were underweight in 2005; AOR 1.37; 95% CI, 1.05–1.80 among those who had a normal BMI in 2005, and AOR 1.49; 95% CI, 1.12–1.97 among participants who had obesity in 2005). On the other hand, cohort members who gained >20% of their baseline weight were more likely to report 'quite a lot' or 'extreme' emotional problems, but this association was statistically significant only among cohort members who were underweight in 2005 (AOR 1.64; 95% CI, 1.15–2.32) and those who had obesity in 2005 (AOR 1.62; 95% CI, 1.07–2.46).

Discussion

Based on our longitudinal study, we were able to confirm that 8-year weight change associates with adverse health outcomes among adults in Thailand. The results also show that weight loss is associated with poor emotional health, especially among cohort members who were underweight at baseline. This study also found that weight gain was associated with poor overall health, poor emotional well-being, and lower levels of energy. These associations were particularly evident among Thai cohort participants who were overweight or had obesity at baseline.

Limited longitudinal evidence is available from low- and middle-income countries, but our findings were in line with those

Table 2
Longitudinal weight change and health outcomes by baseline body mass index categories for Thai cohort study participants between 2005 and 2013.

Weight change by 2013 outcomes[a]	Odds Ratio[b] [95% CI] of adverse outcomes for 8-year longitudinal weight change by baseline body mass index categories[c]			
	Underweight (n = 2876)	Normal (n = 14,059)	Overweight (n = 4277)	Obese (n = 4079)
Overall health (poor, 5.7%)				
$\Delta \leq -5\%$	1.22 [0.43–3.51]	1.33 [0.89–2.01]	1.36 [0.78–2.40]	1.33 [0.88–2.02]
$-5\% < \Delta \leq 5\%$	Reference	Reference	Reference	Reference
$5\% < \Delta \leq 10\%$	0.78 [0.56–1.08]	1.12 [0.96–1.31]	0.97 [0.73–1.29]	1.13 [0.89–1.45]
$10\% < \Delta \leq 20\%$	1.03 [0.69–1.55]	**1.39** [1.13–1.71]	**1.53** [1.01–2.29]	**2.47** [1.74–3.51]
$\Delta > 20\%$	1.08 [0.63–1.85]	**1.44** [1.09–1.90]	**1.82** [1.04–3.19]	**3.20** [2.00–5.16]
Energy (little or none, 8.9%)				
$\Delta \leq -5\%$	0.84 [0.34–2.06]	**1.40** [1.06–1.85]	0.74 [0.46–1.18]	0.83 [0.61–1.12]
$-5\% < \Delta \leq 5\%$	Reference	Reference	Reference	Reference
$5\% < \Delta \leq 10\%$	0.78 [0.56–1.08]	1.12 [0.96–1.31]	0.97 [0.73–1.29]	1.13 [0.89–1.45]
$10\% < \Delta \leq 20\%$	1.12 [0.85–1.47]	**1.32** [1.14–1.52]	1.11 [0.84–1.47]	1.24 [0.97–1.61]
$\Delta > 20\%$	1.22 [0.85–1.74]	**1.36** [1.11–1.65]	1.30 [0.87–1.93]	**1.93** [1.38–2.71]
Emotion (quite a lot, 9.6%)				
$\Delta \leq -5\%$	**1.98** [1.01–1.62]	**1.37** [1.05–1.80]	1.08 [0.72–1.62]	**1.49** [1.12–1.97]
$-5\% < \Delta \leq 5\%$	Reference	Reference	Reference	Reference
$5\% < \Delta \leq 10\%$	0.98 [0.72–1.35]	0.95 [0.82–1.10]	0.76 [0.56–1.04]	1.10 [0.84–1.45]
$10\% < \Delta \leq 20\%$	1.09 [0.82–1.47]	1.02 [0.89–1.19]	1.11 [0.84–1.48]	1.29 [0.97–1.71]
$\Delta > 20\%$	**1.64** [1.15–2.32]	1.07 [0.87–1.30]	1.26 [0.72–1.62]	**1.62** [1.07–2.46]

Bold values indicate statistically significance results when 95% confidence level does not contain the null hypothesis value.
CI, confidence interval.
[a] Adverse outcomes in 2013 were: 'poor or very poor' overall health; 'little or none' energy; and 'quite a lot or extreme' emotional problems.
[b] Adjusted for 2005 baseline age, sex, monthly personal income; and 2005–2016 residence.
[c] Each multivariate analysis excluded cohort members with adverse SF-8 health outcomes at 2005 baseline.

on the impact of weight change on adverse health from a 7-year cohort study of adults in Germany,[16] an 8-year prospective cohort study among adults in Sweden,[17] and a 10-year longitudinal study in the Netherlands[18]; these studies all revealed that weight gain was associated with lower functional health and quality of life, especially among adults who were overweight or had obesity.

Excess weight gain in early adulthood has been reported to have adverse effects in high-income Asian countries. A 5-year longitudinal cohort showed an effect of weight change and incident diabetes among Korean adults,[19] and heavy weight gain has been associated with coronary heart diseases[20] and cancers,[21] even among non-obese Japanese adults. Our findings have added to the evidence that weight change has negative effects on health outcomes in a middle-income Asian setting.

Among the Thai Cohort Study cohort, young females gained the most weight between 2005 and 2013, so they are at an increased risk of poorer health outcomes, a finding that is consistent with the findings from the national health examination survey on the high prevalence of overweight and obesity among females, who already have an increased metabolic risk among the Thai population.[22] This group could be targeted with gender-specific campaigns to promote gradual, well-managed (rather than rapid) weight loss. The population, more generally, could be alerted to the deleterious effects of rapid weight change on physical and emotional health and energy levels, as a better understanding of these health risks could improve weight management strategies. This study points to the importance of preventing weight gain and future non-communicable diseases by focusing on weight maintenance and early healthy lifestyles throughout the lifecourse.[23]

In interpreting our findings, some limitations should be considered. Notably, weight and height in this study were self-reported. However, another related study based on the same study population noted that correlations between measured and self-reported weight and height were high in both sexes, ranging from 0.91 to 0.95.[24] For longitudinal observation, weight change was observed from BMI reported at the 2005 baseline and 2013 follow-up, so there could be fluctuation in weight between these time points that were not accounted for in the analyses. We also could not assess if the weight change was intentional or not. In the final analyses, we excluded cohort members who reported adverse outcomes at baseline to minimize the reverse causation between weight change and health effects.

Our study found that weight change, in particular weight gain, was associated with negative health outcomes, and this effect appeared to increase at higher levels of body size. Future health promotion initiatives to improve health outcomes should focus on preventing weight gain and subsequent adverse health effects, especially among young adults, who appear to have larger fluctuations in weight than older adults.

Conflicts of interest

None declared.

Acknowledgements

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10.5 Appendix E -2013 Thai Cohort Study protocol in English

Questionnaire

Thai Health Research Project 2013

Dear Thai Cohort Study members

With all of your much valued help our Thai Health Research Project has achieved substantial success. Analysing the information you have provided in your questionnaire responses has helped us understand better the risks to Thai peoples' health.

It is now time for us to follow up again on the health of our members. The further information you provide here will help us assess the health of Thai people and be of benefit to all of Thai society. The project follows strict ethical standards and all of your personal information will be held in the strictest confidence. Your name and address will be kept separately from your other data and will only be used to contact you. Your continued involvement in this project is completely voluntary, and if you wish to withdraw at any time please inform us.

If **you are the person whose name appears on the document above** and you are willing to continue participating in this health research project based at Sukhothai Thammathirat Open University please write your name and sign this form below. When you have completed the questionnaire please return it in the envelope included here. You do not need to attach a stamp.

(Name)..... Date...../...../.....

(Mr/Mrs/Miss .....)

If you have any doubts or concerns or need more information on the project please contact us on 02-5047780 during business hours. Thanks and regards.

(Associate Professor Sam-ang Seubsman)

Director Thai Health Research Project

This page will be separated and treated as confidential

Your assistance in filling out this form is very important for the success of our research project. We need to know if your name, address or other details have changed from those shown on the front of the envelope.

Have you changed your **name-surname, address or telephone number from those shown on the front cover of this questionnaire?**

Please **place a cross ✕ in the appropriate boxes ❑. Please use a blue or black pen**

❑ **Have not changed** name-surname, address or telephone number → **Please go to the instructions at the top of the next page**

❑ **There has been a change** to my personal information as follows

❑ **Name-surname** ❑ **Address** ❑ **Telephone number**

Please give details below

First Name..... Family Name .....

Family Name..... Moo Ban ..... Soi .....

Road..... Tambol/Kwang ..... District/Khet .....

Province..... Postcode ☐☐☐☐☐

Home Tel..... Office Tel.....

Mobile..... Email.....

Other contact person (if we cannot contact you)

First Name..... Family Name .....

Family Name..... Moo Ban ..... Soi .....

Road..... Tambol/Kwang ..... District/Khet .....

Province..... Postcode ☐☐☐☐☐

Home Tel..... Office Tel.....

Mobile.....

Please keep a record of your member code (TCSID) from the front of the envelope to use as a reference in any future communication with the Thai Health Risk Transition Study

This page will be separated and treated as confidential

Instructions: Use **a blue or black pen to put a cross** ✕ in the ❑ next to the selected choice to get to this image ☒. Select one answer **except** when told **"more than** one answer can be given." For numeric answers, write number(s) **clearly** in the box(es) - one number per box. Eg 2 4

A Information on you and your work

A1 Sex ❑ Male ❑ Female

A2 When were you born (*according to your Citizen ID Card*)

☐☐/☐☐/☐☐☐☐

Day Month Year (B.E.)

(eg 1 5/0 1/2 5 1 3 if born 15 January 2513 please put)

A3 Where is your current residence located?

❑ Countryside ❑ City/town

A4 How long have you lived at your current residence?

☐☐ **years** *(eg if you have lived there 3 years please write 0 3 Years)*

A5 How far in kilometres is it from your current residence to each of the following places? (kms)

Distance / Place	Less than 5 kms	5-10 kms.	11-20 kms	More than 20 kms
Supermarket/ minimart	❑	❑	❑	❑
ATM	❑	❑	❑	❑
Hospital	❑	❑	❑	❑
Post office	❑	❑	❑	❑
District office	❑	❑	❑	❑
School	❑	❑	❑	❑
Traffic light	❑	❑	❑	❑
Fresh market	❑	❑	❑	❑
Bus stop	❑	❑	❑	❑
Motorcycle taxi stand	❑	❑	❑	❑
Internet cafe	❑	❑	❑	❑

A6 In the past 5 years, has the area where you currently live become more urbanized?

❑ Yes ❑ No ❑ Unsure

A7 How many people live at your current residence?

☐☐ **people** *(including you)*

(eg if there are 3 people please put 0 3)

A8 At present do you have any paid employment?

❑ Yes ❑ No → Go to question **A14**

A9 At present how many hours of paid work do you do per week? ☐☐☐ **hours/week**

A10 How secure do you feel about your job or career future in your current occupation?

❑ Not at all secure ❑ Moderately secure

❑ Secure ❑ Extremely secure

A11 Which of the following best describes your primary occupation? *(Please choose only one answer)*

❑ Senior manager ❑ Middle manager

❑ Professional (eg accountant, doctor, academic)

❑ Skilled worker (eg carpenters, hairdresser, craftsman)

❑ Office assistant

❑ Agricultural or fisheries worker

❑ Factory or assembly worker

❑ Elementary worker (non-physical) (eg courier)

❑ Elementary worker (physical) (eg construction)

❑ Other, please explain……

❶

A12 In the past 12 months, have you experienced uncomfortably hot temperatures in your workplace arising primarily from one of the following causes?

(Please choose only one answer)

- ☐ I am not bothered by high temperatures at work
- ☐ Heat from working outdoors
- ☐ Heat from machinery or production processes
- ☐ Heat from working in a vehicle
- ☐ Heat from work in a stuffy/poorly ventilated building
- ☐ Other, please explain……

A13 In the past 12 months, when you experienced the workplace heat exposure described *in question A12*, **what was your reaction?** *(You may choose more than one answer)*

- ☐ No reaction
- ☐ Mild discomfort
- ☐ Prickly heat/ heat rash
- ☐ Headache/migraine
- ☐ Nausea or vomiting
- ☐ Severe dehydration
- ☐ Dizziness/ fainting with sweating
- ☐ Heat stroke (disorientation /elevated body temp but no sweating)
- ☐ Muscle cramps
- ☐ Low blood pressure

A14 What is your personal average monthly income?

- ☐ ≤3,000 baht
- ☐ 3,001 - 7,000 baht
- ☐ 7,001 - 10,000 baht
- ☐ 10,001 - 20,000 baht
- ☐ 20,001 - 30,000 baht
- ☐ > 30,000 baht

A15 What is your household's average monthly income?

- ☐ ≤3,000 baht
- ☐ 3,001 - 7,000 baht
- ☐ 7,001 - 10,000 baht
- ☐ 10,001 - 20,000 baht
- ☐ 20,001 - 30,000 baht
- ☐ > 30,000 baht

A16 What is your highest level of education (*not including any current studies***)?**

- ☐ Junior high school or equivalent
- ☐ Completed high school or equivalent
- ☐ Post-high school diploma or certificate
- ☐ Bachelor or higher university degree

A17 What is your current marital status? (*Please choose only one answer***)**

- ☐ First marriage
- ☐ Remarried

} Go to question **A19**

- ☐ Separated (but not divorced)
- ☐ Divorced ☐ Widowed ☐ Never married

A18 If not currently married, do you have a partner?

- ☐ Yes and we live together ☐ Yes but don't live
- ☐ Don't have a partner

A19 How tall are you? ☐☐☐ **cms** *(without shoes)*

A20 What is your weight now? ☐☐☐ **kgs**

(eg if your weight is 62 kgs write 0 6 2 *)*

A21 Do you currently care for a chronically ill/disabled/ or frail family member or other person you know?

☐ Yes ☐ No → Go to question **B1**

A22 How many hours per week do you care for this chronically ill/disabled/or frail person?

☐☐☐ **hours/ week**

A23 How many years have you cared for the person mentioned above? ☐☐ **years**

A24 What type/s of care do you provide to the person mentioned above?

(You may choose more than one answer)

- ☐ Help prepare food or eat
- ☐ Help bathe ☐ Help getting dressed
- ☐ Mobility (moving the person)
- ☐ Help going to temples/attending religious activities
- ☐ Shopping and/or providing daily food
- ☐ Emotional support/cheering up
- ☐ Cognitive care (helping to understand)
- ☐ Financial support ☐ Other

❷

B Your general health

B1 Overall how would you rate your health in the <u>past 4 weeks</u>?

❑ Excellent ❑ Very good ❑ Good
❑ Fair ❑ Poor ❑ Very poor

B2 During the <u>past 4 weeks</u>, how much did physical health problems limit your usual physical activities *(such as walking or climbing stairs)***?**

❑ Not at all ❑ Very little
❑ Some ❑ Quite a lot
❑ Could not do physical activities

B3 During the <u>past 4 weeks</u>, how much difficulty did you have doing your daily work, both at home and away from home, because of your physical health?

❑ None at all ❑ A little bit
❑ Some ❑ Quite a lot
❑ Could not do daily work

B4 How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?

❑ None ❑ Very mild ❑ Mild
❑ Moderate ❑ Severe ❑ Very severe

B5 During the <u>past 4 weeks</u>, how much energy did you have?

❑ Very much ❑ Quite a lot ❑ Some
❑ A little ❑ None

B6 During the <u>past 4 weeks</u>, how much did your physical health or emotional problems limit your usual social activities with family or friends?

❑ Not at all ❑ Very little
❑ Somewhat ❑ Quite a lot
❑ Could not do social activities

B7 During the <u>past 4 weeks</u>, how much have you been bothered by emotional problems *(such as feeling anxious, depressed or irritable)***?**

❑ Not at all ❑ Slightly ❑ Moderately
❑ Quite a lot ❑ Extremely

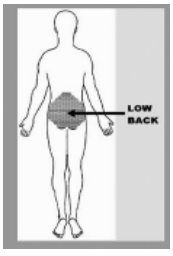
B8 During the <u>past 4 weeks</u>, how much did personal or emotional problems <u>keep you from</u> doing your usual work, school or other daily activities?

❑ Not at all ❑ Very little
❑ Somewhat ❑ Quite a lot
❑ Could not do daily activities

B9 In the <u>past 4 weeks</u>, to what extent has your health limited you in any of the following physical activities?

Limitation for the following physical activities	Not at all	A little	A lot
Climbing a flight of stairs	❑	❑	❑
Walking one hundred metres	❑	❑	❑
Bending, kneeling or stooping	❑	❑	❑
Dressing yourself	❑	❑	❑

B10 In the <u>past 4 weeks</u>, have you had pain in your low back *(in the area shown in the diagram)***?**



❑ Yes

❑ No → Go to question **B12**

B11 <u>If yes</u>, was this pain bad enough <u>to limit</u> your usual activities or change your daily routine for more than one day?

❑ Yes ❑ No

B12 Adults can have up to 32 natural teeth. How many of your own teeth do you have?

❑ None ❑ 1-5 teeth
❑ 6-19 teeth ❑ 20 teeth or more

B13 Do your teeth or dentures currently cause you….

(You may choose more than one answer)

❑ Discomfort speaking ❑ Discomfort swallowing
❑ Discomfort chewing ❑ Loss of social confidence
❑ Pain ❑ None of these

C Your Life

C1 How much support do you feel you get from each of the following groups. *(please place a cross ✕ in the box which best applies to you for each question)*

	Very little	A little	Quite a lot	A lot	Not applicable
Family	❑	❑	❑	❑	❑
Neighbours	❑	❑	❑	❑	❑
Friends	❑	❑	❑	❑	❑
Employee/ supervisor	❑	❑	❑	❑	❑

C2 In the <u>past 4 weeks</u> how much of the time did you feel…? *(please place a cross ✕ in the box which fits best for each question)*

Your feelings *(in the past 4 weeks)*	All of the time	Most of the time	Some of the time	A little of the time	None of the time
…so sad nothing could cheer you up?	❑	❑	❑	❑	❑
…nervous?	❑	❑	❑	❑	❑
…restless or fidgety?	❑	❑	❑	❑	❑
…hopeless?	❑	❑	❑	❑	❑
…everything was an effort?	❑	❑	❑	❑	❑
…worthless?	❑	❑	❑	❑	❑
…happy?	❑	❑	❑	❑	❑

C3 How often do you feel self-conscious or worried in the company of others because of your weight?

❑ Often ❑ Sometimes ❑ Never

C4 Regarding your current body size: Do you feel you need to

❑ Gain weight ❑ Lose weight ❑ Stay the same

C5 In the <u>past 12 months</u>, have you modified your diet to ❑ Gain weight ❑ Lose weight ❑ Did not modify diet

C6 How often do you have trouble controlling your food intake? ❑ Often ❑ Sometimes ❑ Never

❹

C7 Thinking about your own life and personal circumstances, how satisfied are you with…

(Cross box on 0 ⟶ 10 scale that fits best for each question)

Satisfaction with:	Completely Dissatisfied ⟷ Completely Satisfied										
	0	1	2	3	4	5	6	7	8	9	10
…your standard of living?	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑
…how safe you feel?	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑
…feeling part of your community?	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑
…your life as a whole?	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑
…the amount of spare time you have?	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑

C8 Generally speaking, how much would you say that most people can be trusted?

❑ Most people can be trusted ❑ You must be wary of people at all times

C9 How much of an effect did <u>the flood crisis in 2011</u> have on your physical possessions *(house or belongings)*?

❑ A lot ❑ Some effect ❑ Little effect ❑ No effect

C10 How much of an effect did <u>the flood crisis in 2011</u> have on your mental health?

❑ A lot ❑ Some effect ❑ Little effect ❑ No effect

C11 In general <u>in 2012</u> what impact have floods had on you when compared with 2011?

❑ More than 2011 ❑ Less than 2011 ❑ About the same as 2011 ❑ Did not have any effect

D Your food and physical activity

D1 How many serves of vegetables do you eat per day? ☐☐ **serves/day** *Eg if you eat 3 per day please put* 0 3

(for vegetables 1 serve = 1/2 cup of cooked vegetables or 1 cup of raw vegetables)

D2 How many serves of fruit do you eat per day? ☐☐ **serves/day** *Eg if you eat 5serves per day please put* 0 5

(for fruit 1 serve = 1 banana, 1 slice of papaya or 1 cup of diced pieces of fruit)

D3 How many teaspoons of fish sauce do you add to your food in an average day? ☐☐ **teaspoons per day**

if you don't add fish sauce at all please put 0 0

D4 How many teaspoons of sugar do you add to your meals and drinks in an average day? ☐☐ **teaspoons per day**

if you don't add sugar at all please put 0 0

D5 Have you ever seen "nutrition labels" on food?

❑ I have seen them and have read them ❑ I have seen them but have not yet read one ❑ I am unaware of them

D6 How often do you use information from nutrition labels on food products to assist your food purchasing decisions?

❑ Every time I shop ❑ Often ❑ Sometimes

❑ Seldom ❑ Never

❺

D7 How well do you understand the information presented on food "nutrition labels"?

❑ I understand fully ❑ I understand most of the information

❑ I understand some of the information ❑ I do not understand the information but I know it has

❑ I don't understand the information or its potential benefit

D8 Would you like to see more nutrition labeling on foods?

❑ Yes ❑ No ❑ Don't know

D9 On average how often do you eat the following types of food? (*Please cross the one box which fits best for each food type)*

	Never or less than monthly	1-3 times/month	1-2 times/week	3-6 times/week	Daily or more
Food or dessert with coconut milk	❑	❑	❑	❑	❑
Deep fried food	❑	❑	❑	❑	❑
Instant foods eg instant noodles	❑	❑	❑	❑	❑
Fermented/ salted raw food eg crab, fish	❑	❑	❑	❑	❑
Fermented fruit/ vegetable	❑	❑	❑	❑	❑
White rice or white sticky rice	❑	❑	❑	❑	❑
Brown or combined brown and white rice	❑	❑	❑	❑	❑
Fish and fish products	❑	❑	❑	❑	❑
Soft drink (eg 7-Up, coke, pepsi)	❑	❑	❑	❑	❑
Other sweetened drinks (eg iced tea or coffee, sweetened herb drinks)	❑	❑	❑	❑	❑
Milk – fresh, carton or powder	❑	❑	❑	❑	❑
Vitamins or food supplements	❑	❑	❑	❑	❑
Fast food (Western style/farang) eg hamburger, pizza	❑	❑	❑	❑	❑
Western bakery products eg cake, cookies	❑	❑	❑	❑	❑

D10 On your past normal day (ie not a day off or weekend)**, how many times did you have a meal?** ☐☐ **times/day**

(please include meals and snacks)

D11 In the <u>past 7 days</u>, how many times did you eat a main meal alone? ☐☐ **times/day**

D12 When you eat alone do you eat more, less or the same as when you eat with others?

❑ More ❑ Less ❑ About the same

❻

D13 How much of the following types of exercise do you do in a typical week?

(If you exercise 3 times per week please put 0 3 *If you don't do that type of exercise at all please put* 0 0 *)*

Walking continuously <u>for at least 10 minutes</u> *(for work, recreation, exercise or to get from place to place)*	☐☐ times per week
Vigorous physical activities for <u>more than 20 minutes</u> *(that made you breathe harder or puff and pant)*	☐☐ times per week
Moderate physical activities for <u>more than 20 minutes</u> *(like social tennis, golf, gentle swimming or work around the house or other work)*	☐☐ times per week

D14 How often do you do household cleaning or gardening work?

☐ Seldom or never ☐ 1-3 times/month ☐ Once or twice/week

☐ 3-4 times/week ☐ Everyday or almost everyday

D15 How many hours per day (ie per 24 hours) do you <u>usually</u> spend on the following activities?

Activities	Duration
Standing for any purpose at all *(eg for work, while socializing etc.)*	☐☐ hours/day
Sitting for any purpose *(eg reading, resting, writing, thinking, TV, or computer)*	☐☐ hours/day
Sleeping *(if you regularly sleep during the day include this also)*	☐☐ hours/day
Watching TV and/or playing computer games?	☐☐ hours/day

E Your injuries

Your injuries – traffic related

E1 In the <u>past 12 months</u>, how many times did you get injured in a traffic crash

☐ Never → Go to question **E7**

☐ One ☐ Two

☐ Three ☐ Four or more

E2 When you experienced your <u>most serious</u> traffic related injury did you receive medical care?

☐ Yes ☐ No

E3 Did this injury <u>limit</u> your normal activities for one day or more?

☐ Yes ☐ No

E4 When this injury occurred what was your role?

☐ Driver ☐ Passenger

☐ Pedestrian → Go to question **E6**

E5 Type of vehicle you were in or on as driver or passenger?

☐ Bicycle ☐ Motorbike

☐ Bus, van, tour coach

☐ Car/pick-up ☐ Other (eg train, plane, boat)

❼

E6 What was the other party in the collision causing the traffic-related injury?

- ☐ Bicycle
- ☐ Motorbike
- ☐ Bus, van, tour coach
- ☐ Car/pick-up
- ☐ Other vehicle (eg train, boat)
- ☐ Pedestrian
- ☐ Animal (eg dog)
- ☐ Other object not vehicle (eg tree, road, wall)

Your injuries – non-traffic-related

E7 In the past 12 months, how many times did you have a NON-TRAFFIC injury?

- ☐ Never → Go to question **F1**
- ☐ One
- ☐ Two
- ☐ Three
- ☐ Four or more

E8 When you experienced your most serious non-traffic-related injury did you receive medical care?

- ☐ Yes
- ☐ No

E9 Did this injury limit your normal activities for one day or more?

- ☐ Yes
- ☐ No

E10 How were you injured?

- ☐ Assault (punch, push or kick)
- ☐ Other blunt (non-sharp) force
- ☐ Stab/cut
- ☐ Gunshot
- ☐ Fall (not pushed)
- ☐ Lifting heavy obje
- ☐ Fire, heat, scald
- ☐ Near-drowning
- ☐ Bite or sting (animal, insect)
- ☐ Poisoning
- ☐ Choking
- ☐ Other

E11 What was the location at which your most serious non-traffic related injury occurred?

- ☐ Home
- ☐ Sports facility
- ☐ Workplace (agricultural)
- ☐ Workplace (non-agricultural)
- ☐ Other

E12 What was the nature of your most serious non-traffic injury? *(You may choose more than one answer)*

- ☐ Fracture
- ☐ Sprain, strain or dislocation
- ☐ Cut, bite or open wound
- ☐ Bruise or superficial injury
- ☐ Burn/scald
- ☐ Concussion
- ☐ Organ system (internal) injury
- ☐ Other

E13 How did this non-traffic injury occur?

(Please choose only one answer)

- ☐ Unintentional/ accident
- ☐ Intentional by another person
- ☐ Intentional (not involving another person)

F Your Health History

F1 Have you ever received a <u>confirmed diagnosis</u> from a doctor that you <u>definitely have</u> any of the following diseases?

Health condition	Definitely have disease	Doctor said I am <u>at risk</u> of the disease	Don't have the disease
Diabetes	❑	❑	❑
High cholesterol/high blood lipids	❑	❑	❑
High blood pressure	❑	❑	❑
Ischemic (coronary) heart disease	❑	❑	❑
Cerebrovascular disease (stroke)	❑	❑	❑
Liver cancer	❑	❑	❑
Lung cancer	❑	❑	❑
Stomach cancer	❑	❑	❑
Colon-rectum cancer	❑	❑	❑
Breast cancer	❑	❑	❑
Other cancers	❑	❑	❑
Kidney disease	❑	❑	❑
Other disease (specify)……	❑	❑	❑

F2 What health insurance scheme/s covers you <u>at present</u> and for how long have you been covered? (*please cross all boxes which apply***)(***If you have been covered by a scheme for less than one year please put* **0 1** *)*

Type of health insurance	Length of coverage
❑ Don't have insurance	
❑ Civil Servants Coverage scheme	☐☐ Years
❑ Employer provided coverage	☐☐ Years
❑ Private health insurance	☐☐ Years
❑ Social Security Scheme	☐☐ Years
❑ Universal Coverage Scheme	☐☐ Years
❑ Other.....	☐☐ Years

F3 In the <u>past 12 months</u> how many times have you used the following types of health services? *(You may choose more than one answer)*

Health service type	Number of visits (past 12 months) Eg if you visited once in the past year please put 0 1 times
Government health centre	☐☐ times
Community hospital	☐☐ times
Private health clinic	☐☐ times
Government hospital	☐☐ times
Private hospital	☐☐ times
Traditional medicine	☐☐ times
Pharmacy	☐☐ times
Other.....	☐☐ times

❾

G Smoking, alcohol and transport

G1 Are you a <u>current</u> smoker?

❑ No ❑ Yes and I smoke ☐☐ cigarettes per day

G2 Please describe your current alcohol drinking?

❑ Don't drink ❑ Used to drink but quit

❑ Drink in social situations, about ☐☐ glasses/week

❑ Current regular drinker of about ☐☐ glasses/ day

G3 In the <u>past 12 months</u> have you ever driven a vehicle after consuming 3 or more glasses of alcohol?

❑ Yes ❑ No

❑ Don't normally drive

G4 In the <u>past 12 months</u>, for personal transport how often did you…?

	Always	Sometimes	Never	Not applicable	
Use car safety belt (<u>front seat</u>)	❑	❑	❑	❑	No safety belt or don't ride in front seat
Use car safety belt (<u>back seat</u>)	❑	❑	❑	❑	No safety belt or don't ride in back seat
Ride on back step of "song thaew"	❑	❑	❑	❑	Don't use "song thaew"
Ride in back of open truck/pick up	❑	❑	❑	❑	Don't use such vehicle
Use motorcycle helmet	❑	❑	❑	❑	Don't use motorcycle
Ride on motorcycle with 3 or more people	❑	❑	❑	❑	Don't use motorcycle

H Birth and contraception *(for cohort member women only to answer)*

(Male cohort members please ignore this section)

H1 How many babies have you ever given birth to? ☐☐ **Babies** *(If you have never given birth please put* **0 0** *)*

H2 Please tell us about your past and present use of the following contraceptives *(*If you have used for less than one year please put **0 0** *)*

Have you ever taken or used the following types of hormonal contraceptives?		Age started using?	Age past used? (*or age now if still using*)	How long did you use it altogether? (*don't count periods of non-use)*
Oral contraceptive pill	❑ No ❑ Yes →	☐☐ yrs	☐☐ yrs	☐☐ yrs
Injections every three months (depo provera)	❑ No ❑ Yes →	☐☐ yrs	☐☐ yrs	☐☐ yrs
Contraceptive implant under the skin (may past 3-5 years)	❑ No ❑ Yes →	☐☐ yrs	☐☐ yrs	☐☐ yrs

⑩

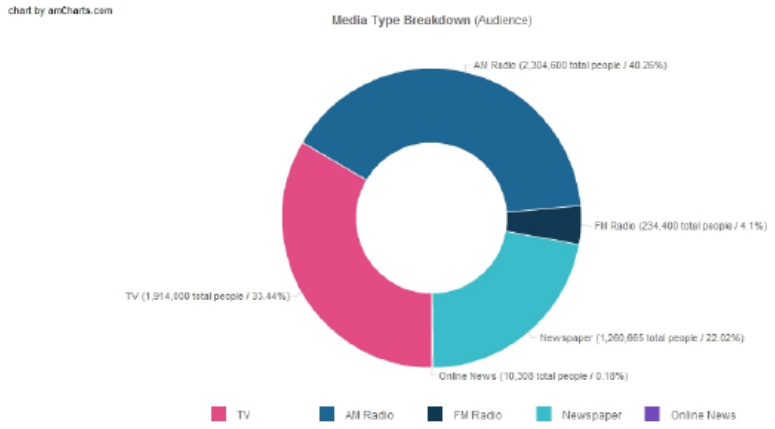
Thank you very much for your kind cooperation

10.6 Appendix F – Media report summary for Chapter 5

MON 17 JULY 2017

7 JULY (3) - SUGAR - MEDIA ANALYTICS REPORT

Total media types	Total items	Total audience
5	79	5,723,973



> An analysis of coverage produced in the 14 days between 04-07-2017 and 17-07-2017 from 1 folders found 79 items. This coverage reached a cumulative audience of 5,723,973.

07 Jul 2017
Herald Sun, Melbourne

Author: LANAI SCARR • Section: General News • Article type : News Item
Classification : Capital City Daily • Audience : 316,499 • Page: 7
Printed Size: 757.00cm² • Market: VIC • Country: Australia • ASR: AUD 42,033
Words: 632 • Item ID: 805860091

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Interview with Keren Papier, Australian National University. ...

3AW, Melbourne, Breakfast, Kate Stevenson and Justin Smith — 07 Jul 2017 8:07 AM

Duration: 2 mins 48 secs • VIC • Australia • 7 JULY - SUGAR - PAPIER • ID: M00070985159

Interview with Keren Papier, Australian National University.
Smith says sugary drinks can cause type 2 diabetes. Papier says the study is telling them that consuming sugary drinks is likely to increase the risk of diabetes independently of weight gain or obesity. Smith points out the story includes a chocolate milk and orange juice. Papier says sugary drinks do include sports drinks, sweetened milk and fruit juices with added sugar. She suggests everyone should try to reduce their sugary drink consumption. Papier explains the World Health Organisation recommends that they cut their sugar intake to less than 5% sugar a day.

Audience

214,000 ALL, 89,000 MALE 16+, 122,000 FEMALE 16+

Interviewees

Keren Papier, Australian National University

Report by Caroline Winter, ABC. Australian researchers have found that drinking sugary ...

Radio National, Canberra, The World Today, Thomas Oriti — 07 Jul 2017 12:36 PM

Duration: 3 mins 59 secs • National • Australia • 7 JULY - SUGAR - PAPIER • ID: X00070993056

Report by Caroline Winter, ABC. Australian researchers have found that drinking sugary drinks increases the risk of diabetes, independent of obesity. The Australian National University study also revealed that women who consumed sugar-laden drinks are at much higher risk than men. Researchers say a reduction in sugary drink consumption is likely reduce rates of diabetes in Australia and the study bolsters calls for a sugar tax. Karen Papier, Australian National University, says that study showed that women react differently to sugar-filled drinks and are more likely to develop Type II diabetes from regular consumption. Dr Michael Gannon, President AMA, says that the study does not prove that high-doses of sugar cause diabetes. He says that a sugar tax needs to be implemented in Australia. Geoff Parker, CEO Australian Beverage Council, says that research shows that sugary drinks are not the primary driver of poor diets.

Audience

177,300 ALL, 98,500 MALE 16+, 78,800 FEMALE 16+

Interviewees

Dr Michael Gannon, President AMA|Geoff Parker, CEO Australian Beverage Council|Karen Papier, Australian National University

Mentions

CSIRO

Also broadcast from the following 59 stations

ABC Alice Springs (Alice Springs), ABC Ballarat (Ballarat), ABC Broken Hill (Broken Hill), ABC Capricornia (Rockhampton), ABC Central Coast (Erina), ABC Central Victoria (Bendigo), ABC Central West NSW (Orange), ABC Coffs Coast (Coffs Harbour), ABC Esperance (Esperance), ABC Eyre Peninsula and West Coast (Port Lincoln), ABC Far North (Cairns), ABC Gippsland (Sale), ABC Gold Coast (Gold Coast), ABC Goldfields WA (Kalgoorlie), ABC Goulburn Murray (Wodonga), ABC Great Southern (Albany), ABC Great Southern WA (Wagin), ABC Illawarra (Wollongong), ABC Kimberley (Broome), ABC Midwest and Wheatbelt (Geraldton), ABC Mildura - Swan Hill (Mildura), ABC New England North West (Tamworth), ABC Newcastle (Newcastle), ABC North and West SA (Port Pirie), ABC North Coast NSW (Lismore), ABC North Queensland (Townsville), ABC North West Qld (Mt Isa), ABC North West WA (Karratha), ABC Northern Tasmania (Launceston), ABC Radio Adelaide (Adelaide), ABC Radio Brisbane (Brisbane), ABC Radio Canberra (Canberra), ABC Radio Darwin (Darwin), ABC Radio Hobart (Hobart), ABC Radio Melbourne (Melbourne), ABC Radio Perth (Perth), ABC Radio Sydney (Sydney), ABC Riverina (Wagga Wagga), ABC Riverland SA (Renmark), ABC Shepparton (Shepparton), ABC South East NSW (Bega), ABC South East SA (Mt Gambier), ABC South West WA (Bunbury), ABC South Western Victoria (Warrnambool), ABC Southern Queensland (Toowoomba), ABC Sunshine Coast (Sunshine Coast), ABC Tropical North (Mackay), ABC Upper Hunter (Muswellbrook), ABC Western Plains NSW (Dubbo), ABC Western Queensland (Longreach), ABC Western Victoria (Horsham), ABC Wide Bay (Bundaberg), Radio National (Adelaide), Radio National (Darwin), Radio National (Sydney), Radio National (Melbourne), Radio National (Brisbane), Radio National (Hobart), Radio National (Perth)

Interview with Diabetes Australia CEO Greg Johnson on proposed sugar tax. There have ...

Sky News Live, Sydney, News Day, Newsreader — 07 Jul 2017 3:26 PM

Duration: 6 mins 47 secs • National • Australia • 7 JULY - SUGAR - PAPIER • ID: X00070992570

Interview with Diabetes Australia CEO Greg Johnson on proposed sugar tax. There have been further calls for the government to introduce a sugar tax after a study in Thailand has revealed there is a particular correlation between sugary soft drinks and diabetes. Johnson confirms it is a study led by the Australian National University. He says they are calling for a targeted tax or health levy on sweetened beverages. He explains this levy could generate $400m of government revenue that can be directed towards obesity-prevention programs and public education for children in order for them to prevent type 2 diabetes. He says the highest consumption of sugary and sweetened drinks is in children aged between 2yo and 16yo. He says the other area where there is a serious impact of sugary drinks is in Aboriginal and Torres Strait Islander health. He notes these drinks also include health drinks, sports drinks and anything that contain between 12 and 23 teaspoonfuls of sugar in one 600ml drink. He claims the Australian Medical Association, Australian Dental Association and other peak health groups support this as a good targeted measure while there is 70% community support for a tax on sugary and sweetened drinks.

Audience

19,000 ALL, 8,000 MALE 16+, 7,000 FEMALE 16+

Interviewees

Greg Johnson, CEO, Diabetes Australia

Also broadcast from the following 9 stations

Sky News Live (Melbourne), Sky News Live (Canberra), Sky News Live (Brisbane), Sky News Live (Adelaide), Sky News Live (Perth), Sky News Live (Regional NSW), Sky News Live (Regional Queensland), Sky News Live (Regional Victoria), Sky News Live (Tasmania)

08 Jul 2017
Canberra Times, Canberra

Author: Steven Trask • Section: General News • Article type : News Item
Classification : Capital City Daily • Audience : 25,571 • Page: 11
Printed Size: 172.00cm² • Market: ACT • Country: Australia • ASR: AUD 1,368
Words: 328 • Item ID: 806692982

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Health Type 2 diabetes would be slashed

Sugar tax call backed by study

Steven Trask

Calls to impose a controversial sugar tax in Australia have been bolstered by a new study led by researchers from the Australian National University.

The study, performed in Thailand, suggested that thousands of cases of type 2 diabetes could be prevented every year by cutting out sugary drinks.

Lead author Keren Papier, from ANU's Department of Global Health, said the findings could be applicable in Australia.

"A reduction in sugary drink consumption is likely to reduce rates of diabetes in Australia," she said. "Several countries, including Mexico, the United States, France and Chile, have already started acting on sugary drinks by imposing or committing to a sugar tax.

"Findings from the US and Mexico show that applying the tax has led to a 17 and 21 per cent decrease respectively in the purchase of taxed beverages among low-income households."

The results came from the massive Thai Cohort Study, which analysed a nationwide sample of almost 40,000 adults between the years of 2005 and 2013.

Using a statistical technique called mediation analysis, it showed that diabetes risk increased as more sugary drinks were consumed.

"Sugary drinks are an ideal target for public health interventions to help control the type 2 diabetes epidemic since they have no nutritional value and do not protect against disease," Ms Papier said.

"Over 4000 cases of type 2 diabetes could be prevented annually in the Thai population if people avoided drinking sugary drinks daily. Thai women, who are at double the risk of type 2 diabetes from drinking sugary drinks, would be the main beneficiaries."

The sugar tax concept has divided opinion both in Australia and overseas. In February, Assistant Health Minister Dr David Gillespie squashed the idea of introducing a sugar tax.

"Cut to the chase: the thing with all of the proponents of sugar taxes, fat taxes, whatever tax, is taxes will make people angry and it won't change what they eat," he said.

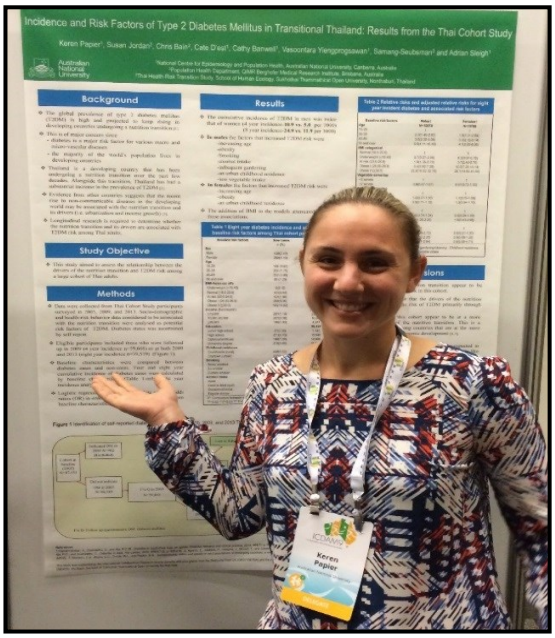
10.7 Appendix G – Thesis photos

This appendix contains photographs from my PhD related activities. These include photographs from: my field work in Thailand, PhD conference presentations, related courses, and relevant media experiences.

2015: Preparing physician telephone interview invitations for TCS participants

2015: Meeting with STOU students in Bangkok

2015: Preparing dietary surveys to be sent out to TCS participants



2015: Presentation at the International Conference on Diet and Activity Methods

2016: Attending the 6th International Course in Nutritional Epidemiology in London

2016: Presentation at the Australian and New Zealand Obesity Society Annual scientific meeting

2017: Channel 10 television interview on sugary drink consumption and type 2 diabetes risk in Thai adults

2017: Media and Outreach Awards ceremony, Australian National University